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RETICULIN CONTENT AND PROGNOSIS IN MALIGNANT MELANOMA OF THE UVEA

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We began an investigation in 1939 into the histopathology of malignant melanoma of the uvea of patients treated at the Glasgow Eye Infirmary during the preceding twenty years. Callender and Wilder [1] and King [2] had published papers in which it appeared that the prognosis was influenced by the reticulin content of the growths. They had observed their patients for five years or over. Pahwa [3] reported on a series of 100 patients observed for six years and found the reticulin content to be a helpful guide in prognosis. Callender, Wilder and Asch [4] have reported on a series of 500 patients observed over five years, and of that number 200 have been observed for ten years. Our investigation was interrupted by the outbreak of war, but we felt that the study of a series of patients for a long period, namely twenty years, would give further information. There were 82 patients with malignant melanoma of the uvea treated at the Glasgow Eye Infirmary between 1919 and 1939. All were written to, and it was then possible to make a grouping of live patients and dead patients. Many of those alive and living at a distance did not come to see us but reported that they were well and at work, which information was considered enough. If the patient was dead, a history was requested of the relatives in person or by mail, and then the family physician was written to, or the hospital in which death had occurred. If these means failed, we wrote to the registrar of deaths for the district in which the patient last resided. The certification of death commonly gave the cause as "secondary carcinoma of the liver." In only a few instances was a report of a postmortem examination available. When the cause of death was uncertain the case was excluded from our series. Some of the blocks had been lost, or only a remnant remained, after former investigators had finished with them. Of the 82 patients with malignant melanoma of the uvea treated in the twenty years, the number for which there were an unequivocal history and a relevant block for section was 41.

We shall describe the methods of silver impregnation of sections, not because originality is claimed for them, but so that the results may be correlated with those of other workers. Most of the many modifications of silver impregnation of reticulin consist of variations in the silver salt. We impregnated all sections several times, first with a solution of silver diaminohydroxide and second with a solution of silver carbonate. We were guided by the extensive researches of

1. Callender, G. R., and Wilder, H. C.: Am. J. Cancer **25**:251-258, 1935.
2. King, E. F.: Tr. Ophth. Soc. U. Kingdom **57**:97-106, 1937.
3. Pahwa, T. R.: Brit. J. Ophth. **25**:241-285, 1941.
4. Callender, G. R.; Wilder, H. C., and Asch, J. E.: Am. J. Ophth. **25**:962-967, 1942.

Gomori [5] into the variants of the method of silver impregnation and their efficacy. The details of the first method of impregnation, by the use of silver diamino-hydroxide, are as follows:

1. Cut sections in paraffin no. 8 to 10 and reduce to water in the ordinary way. Bleach in a 0.5 per cent solution of potassium permanganate to which has been added one part in twenty of 3 per cent sulfuric acid before use. Leave two or three minutes.
2. Rinse in water.
3. Transfer to 2 per cent oxalic acid solution until completely bleached. If there is any persistent pigmentation of a section it must go back into the permanganate solution. This process is the exhaustive oxidation of other writers, and we found it to be essential.
4. Rinse in water.
5. Mordant in 2.5 per cent ferric alum solution for one-half to one minute.
6. Rinse in water.
7. Stain in silver solution for one-half to one minute. This solution is made up as follows: To 10 cc. of 20 per cent silver nitrate add 10 drops of 40 per cent sodium hydroxide and dissolve the precipitate in a strong solution of ammonia (such as stronger ammonia water U. S. P. or strong solution of ammonia B. P.). Do not add the excess. Make up to 50 cc. with distilled water.
8. Rinse in water.
9. Reduce in 10 per cent solution of formaldehyde.
10. Rinse in water.
11. Tone in gold chloride if necessary to clear the background.
12. Rinse in water.
13. Fix in 5 per cent solution of sodium hypothiosulfite.
14. Dehydrate, clear and mount.

We found that with this method sections repeatedly floated off the slides in spite of pretreatment with gelatin and solution of formaldehyde vapor; also, the short exposure in the silver bath made overstaining easy. After trying several silver salts we found that those with a high ammonia content loosened the sections, and we chose a silver carbonate with which to stain the series again. The modification as we employed it differed from the one outlined only in that sections might be sensitized for one to five minutes in ferric alum solution and might remain fifteen to twenty minutes in the silver bath. The silver carbonate solution is made up by adding to 10 cc. of 25 per cent silver nitrate a strong solution of ammonia drop by drop until the precipitate formed disappears. To the solution is added 10 cc. of a 3 per cent solution of sodium carbonate and the whole made up to 200 cc. with distilled water. This is the solution used by Foot [6] except that his is made up to 50 cc. We found that the quarter strength solution never loosened sections without pretreatment, gave a full reticulin picture and did away with the tendency to overstaining. The two modifications gave equally good pictures, and sections which showed a small reticulin content were no fuller by the alternative process. The best results were obtained when all solutions were prepared afresh for each batch of sections and the sections mounted immediately.

In the accompanying tables the complete findings are recorded. The reticulin content is shown as 1 plus to 4 plus, and the four types are shown in the photomicrographs. Figure 1 (1 plus reticulin) shows scanty reticulin, present only at the periphery of the growth and around the blood vessels. Figure 2 (2 + reticulin) shows reticulin at the periphery, becoming interlobular and enclosing ever larger lobules of growth toward the center of the tumor. In figure 3 (3 + reticulin) there is a meshwork that is fairly uniform but not so close as that in figure 4 (4 +

5. Gomori, G.: Am. J. Path. **13**:993-1002, 1937; **15**:493-495, 1939.
6. Foot, N. C.: Am. J. Path. **8**:245-254, 1932.

reticulin) and does not show large reticulin-free lobules like those in figure 2. For the sake of completeness we have included a note of the predominant cell types. The polymorphism of malignant melanoma is well known. The predominant cell type is noted. As we have found spindle B cells associated with spindle A cells elsewhere in the growth, we have classed the cell type as A and B. Spindle A,

TABLE 1.—*Data Concerning Patients Who Are Still Living* *

No.	Sex	Age at Operation	Time of Survival Yr.	Mo.	Cell Type	Pigment Content	Reticulin Content
1	F	40	17	..	A (F)	M1	++++
2	F	52	15	..	A	M1	+++
3	F	47	13	..	A	M1	++++
4	F	43	12	..	A	M1	++++
5	M	42	11	..	A & B	M1	++++
6	M	42	11	..	A & B	M1	+++
7	M	54	10	3	A & B	M2	++
8	F	37	10	..	A	M1	+
9	M	39	10	..	A	M1	+++
10	M	39	9	..	Mx	M1	+++
11	M	65	9	..	Mx	M1	++++
12	M	57	9	..	A	M1	++++
13	M	45	9	..	A (F)	M1	++++
14	M	36	9	..	A	M1	+++
15	F	52	8	..	A	M1	+
16	F	74	5	8	A	M4	++
17	F	49	5	4	A (F)	M2	+++
18	M	67	4	9	A	M3	++
19	F	61	4	4	Mx	M2	+++

* The patients who were alive in 1939 were writtten to again in 1942.

TABLE 2.—*Data Concerning Patients Who Have Died*

No.	Sex	Age at Operation	Time of Survival Yr.	Mo.	Cell Type	Pigment Content	Reticulin Content
1	M	45	18	..	A	M1	++++
2	F	36	11	..	A	M3	+++
3	M	60	10	.. (S*)	A & B	M1	+
4	M	59	10	.. (S)	A & B	M2	+++
5	M	64	7	.. (S)	A	M1	+++
6	F	46	7	..	A & B	M2	+++
7	F	60	4	5 (S)	Mx	M2	+++
8	F	45	4	3	Ep	M3	++
9	M	68	4	2 (S)	Ep	M2	+++
10	F	77	3	9 (S)	Mx	M3	+
11	F	65	3	4	Mx	M1	+++
12	F	48	3	1 (S)	A & B	M1	+++
13	M	65	2	6 (S)	Mx	M3	++
14	M	41	2	6 (S)	A	M2	++
15	M	39	2	5	Mx	M1	+++
16	M	55	1	8 (S)	Mx	M4	+++
17	F	37	1	6 (S)	A (F)	M1	++
18	M	55	1	4 (S)	Ep	M2	+
19	F	48	1	.. (S)	Mx	M3	+
20	M	52		9 (S)	Mx	M4	++
21	M	59		6 (S)	Mx	M1	+
22	F	62		6	Ep	M1	+++

* S indicates secondary, or metastatic growth.
† F indicates a fascicular arrangement; A, spindle A type cells; B, spindle B type cells; Mx, mixed cells and Ep, epithelioid cells.

spindle B and epithelioid cells are shown in figure 5. A fascicular arrangement was found of spindle cell types and was not accorded a separate classification. The pigment content of the growth is shown as M1 to M4, the numerals indicating only an arbitrary assessment.

The sex distribution was about equal, and the average survival was about eight years. It was easier to trace the patients who had lived a long time than those who had been dead a long time. For the most part the group surviving six to fifteen years showed a fuller reticulin picture than the group surviving up

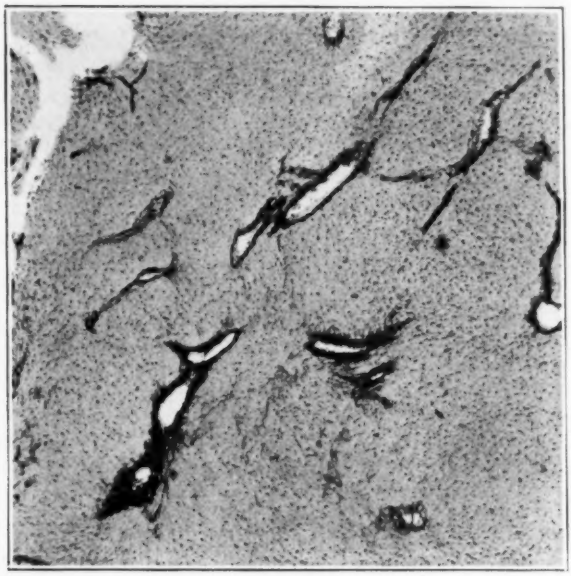

Fig. 1.—Malignant melanoma showing a reticulin content of 1 plus. (Magnification, × 50; silver stain.)

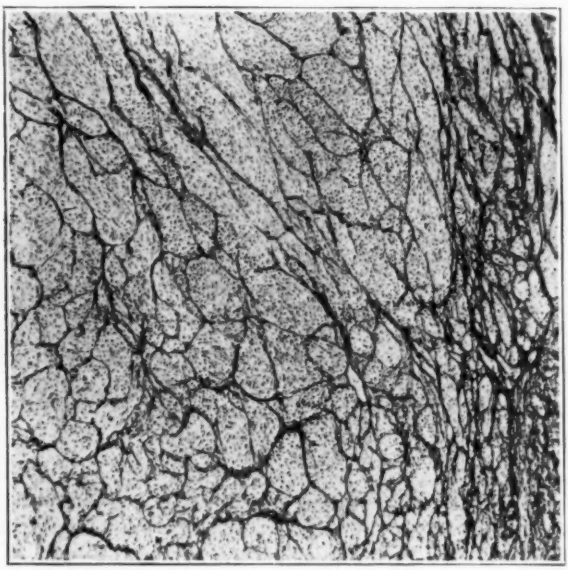

Fig. 2.—Malignant melanoma showing a reticulin content of 2 plus. (Magnification, × 50; silver stain.)

to six years. There were exceptions. Again, in the longer-lived group there was a predominance of the benign spindle A or A and B type of cell, and in the shorter-lived group a predominance of mixed and epithelioid types. To this generalization there were also exceptions. The pigment content was increased

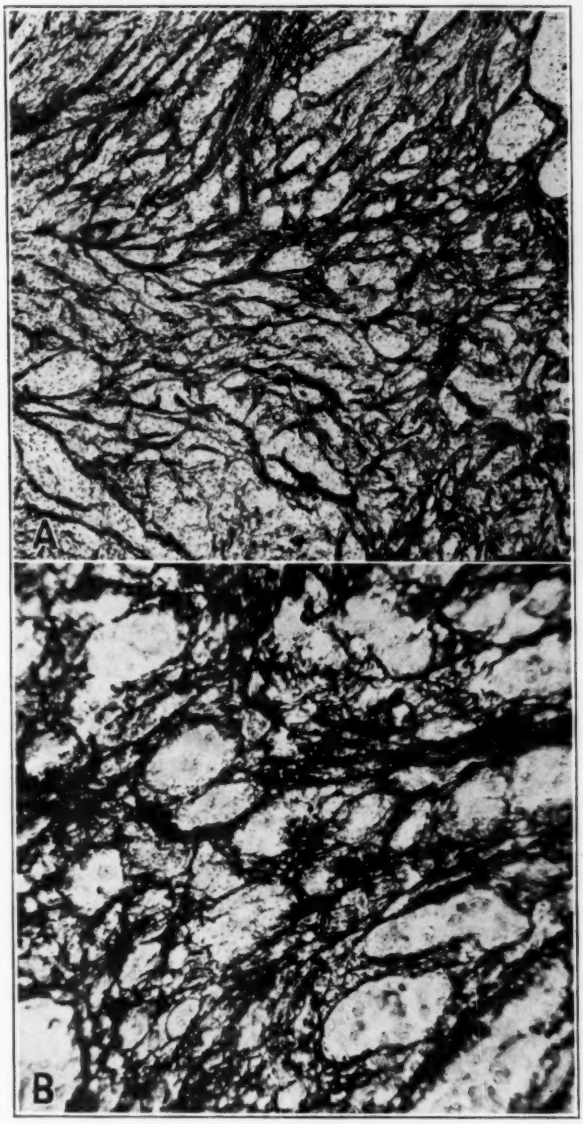

Fig. 3.—Malignant melanoma showing a reticulin content of 3 plus. (Silver stain; *A*, magnification, × 50; *B*, magnification, × 300.)

in the short-lived group. Callender and Wilder [1] found that the spindle cell types were relatively benign and that a full reticulin content was of good import, while epithelioid and mixed cell types and a poor reticulin content were of bad import. Our findings are in general agreement, but we think that the exceptions are important. We do not find that the survival time can be gaged accurately from the

histologic characteristics of cell type, pigment content and reticulin content. Taken together these characteristics usually permit one to say whether the patient will live a long or a short time. Probably the cell type is first in importance, with reticulin content and pigment content as subsidiary factors. We were not able

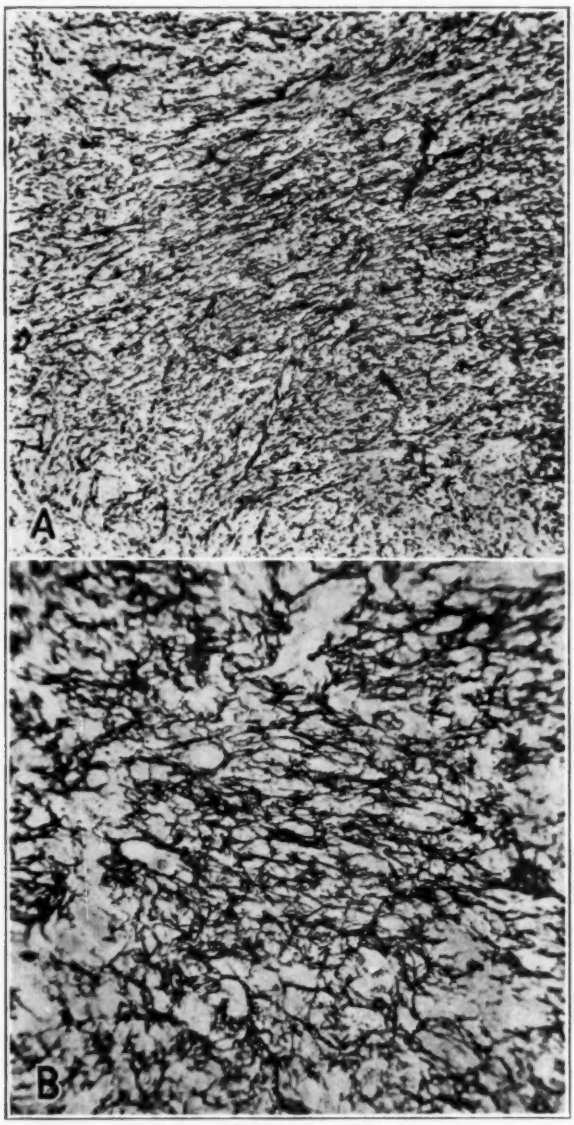

Fig. 4.—Malignant melanoma showing a reticulin content of 4 plus. (Silver stain; *A*, magnification, × 50; *B*, magnification, × 300.)

to correlate histologic changes with the clinical stage of the tumor, the involvement of the scleral veins and the extraocular involvement.

The technic of silver impregnation of reticulin is not the simplest of histologic methods. Gomori [5] stated that there are unaccountable failures, more by some methods than by others. These failures are not frequent in our experience. He

stated that a much fuller reticulin picture is obtained by some methods than by others. In our series of sections stained according to two modifications of technic, reagents being used which he found to give good results, we found the pictures to be the same. Nevertheless, in our investigation we have felt that when the histologic method itself is subject to even occasional failure the demonstration of reticulin by silver impregnation should be interpreted with this in mind when one is assessing the prognosis.

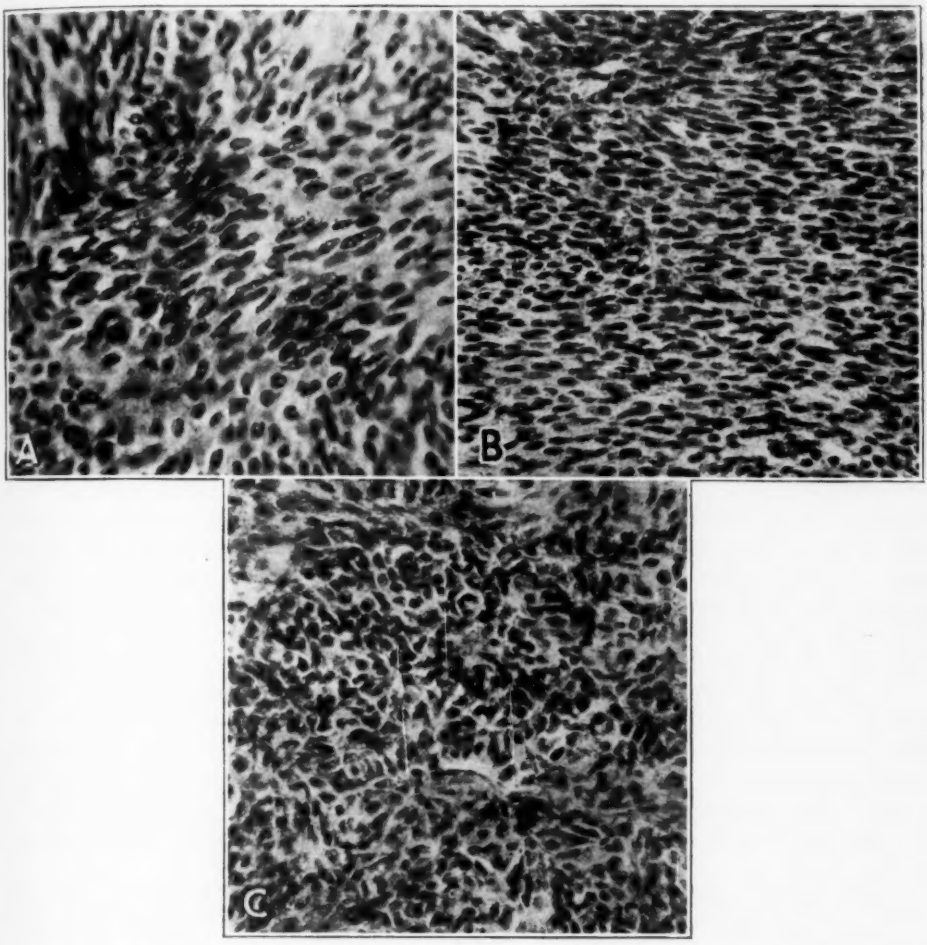

Fig. 5.—*A*, spindle A cells, fascicular arrangement; *B*, spindle B cells; *C*, epithelioid cells. (Hematoxylin and eosin stain; magnification, × 300.)

SUMMARY

Forty-one specimens of malignant melanoma of the uvea from patients seen at the Glasgow Eye Infirmary between 1919 and 1939 have been examined histologically. The patients were followed up, and when death had occurred the cause of death was ascertained. Tables of results are presented. The value of silver impregnation for determination of the reticulin content in assessing the prognosis is discussed, as is the value of study of the cell type and pigment content.

ANISEIKONIA

A REVIEW OF 200 CONSECUTIVE CASES EXAMINED ON THE EIKONOMETER

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There have been a number of excellent and interesting papers written on the theoretic aspects of aniseikonia.[1] There have been a few papers written on the clinical symptoms and the results of treatment.[2] In general, however, these papers have been statistical. One can find a few papers critical of aniseikonia, such as those of Ludvigh,[3] Friedenwald[4] and Edward Jackson.[5] Unfortunately most of these authors apparently wrote at the library table and did not take the necessary time to prove or disprove experimentally many of their statements of physiologic facts. Most of the fundamental ideas expressed in their papers have been proved experimentally to be wrong.

Ophthalmologists as a group have been skeptical in accepting the reported therapeutic results obtained in correcting aniseikonia. Their skepticism is due to a number of causes. First, the symptoms of aniseikonia are purely subjective and therefore might be relieved by suggestion. Second, the symptoms are similar to those of refractive errors or muscular imbalance, the most common being headaches, fatigue of the eyes, car sickness, a tendency to dizziness and nausea, and therefore the relief might be due to a more adequate correction of the refractive errors or muscle imbalances. Third, there are patients who show a relatively large degree of aniseikonia who do not suffer from symptoms, and, also, there are persons who do not show any, or show only very little, aniseikonia but who can tolerate an artificially induced difference in the size of the ocular images without symptoms. Fourth, a number of patients who suffer from the symptoms mentioned and have a considerable size difference are not relieved of their symptoms when their aniseikonia is corrected. This situation, of course, is not unique, as there are many patients with refractive errors or muscle imbalances or a combination of the two whose symptoms are not relieved by the adequate correction of these defects. In spite of such contradictions and inconsistencies, practically every one who has had any first hand clinical experience in caring for patients with aniseikonia is convinced that this is a real defect of binocular vision and causes symptoms which can be abated by the use of proper lenses.

Historically, it is interesting to note that Donders[6] in 1864 pointed out that corrected anisometropia could produce a size difference of the retinal images

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1. Ames, A., Jr.; Ogle, K. N., and Gliddon, G. H.: Corresponding Retinal Points: The Horopter and Size and Shape of Ocular Images, J. Optic. Soc. America **22**:538 (Oct.); 575 (Nov.) 1932. Ogle, K. N.: The Induced Size Effect, ibid. **30**:145-151 (April) 1940.

2. Carleton, E. H., and Madigan, L. F.: Size and Shape of Ocular Images: II. Clinical Significance, Arch. Ophth. **7**:720-738 (May) 1932; Relationships Between Aniseikonia and Ametropia, from a Statistical Study of Clinical Cases, ibid. **18**:237-247 (Aug.) 1937.

3. Ludvigh, E. J.: Aniseikonia, Am. J. Ophth. **19**:282-301 (April) 1936.

4. Friedenwald, S.: Diagnosis and Treatment of Anisophoria, Arch. Ophth. **15**:283-307 (Feb.) 1936.

5. Jackson, E.: Importance of Aniseikonia, Am. J. Ophth. **20**:16-21 (Jan.) 1937.

6. Bielschowsky, A.: Aniseikonia, Acta ophth. **16**:188-227, 1938.

which would disturb or even make impossible single binocular vision. Hess [7] in 1905 advanced the theory that the difficulties which one experiences with glasses which correct the higher degrees of anisometropia are caused by the prismatic effect which occurs when one looks through the peripheral part of such lenses and that the symptoms are not due to the difference in the size of the two ocular images. It is probable that either one of the effects, or a combination of the two, is at fault.

Erggelet [8] (1916) was the first to mention the possibility that a difference in size of the ocular images might have a physiologic origin and that special methods would be required to measure this difference. When one considers the asymmetries which are present in the human body, it is not surprising to find asymmetries existing in the chain between the object and the visual cortex, where the visual impression, known as the ocular image, is perceived. That there is an asymmetric distribution of the visual elements in the nasal and temporal halves of the two retinas, and that this asymmetry is not the same in all persons, is shown by the contradictory results of the Kundt and Munsterberg [9] experiments in bisection of a straight line. That there may also be an asymmetry in the distribution of the sensory elements between the two eyes can be demonstrated by the rotation of the longitudinal horopter [10] for symmetric convergence about the point of fixation. This rotation is always toward the eye with the larger ocular image.

No clinical method has been developed which would enable one to measure the asymmetry between the two halves of the retina. However, through the research of Ames, Gliddon and Ogle a satisfactory method for measuring the asymmetry between the ocular images of the two eyes has been developed. The original instrument was a glorified haploscope which gained the name "Spirit of Hanover." Refinements and simplifications in this complicated laboratory instrument have resulted in the eikonometer, which is in use today for the clinical detection and measurement of aniseikonia. As a rule the type and amount of aniseikonia which exist in any person are fairly constant, as has been shown by repeated tests at various intervals. Likewise, the character of the size difference is usually similar for both distant and near vision. Patients representing exceptions to the general rule will be discussed later.

The only patients who have been subjected to examinations with the eikonometer are those who have not been relieved of their symptoms by wearing lenses to correct their refractive errors or muscle imbalances or a combination of the two. Most of these patients have been seen by several ophthalmologists and have had many pairs of glasses, none of which relieved them of their symptoms. All have undergone one or more physical and laboratory examinations which gave negative results. Thus, the patients who form the basis of this report are physically sound persons who have continued to suffer from headache, pain in the eyes, ocular fatigue (especially after close work) and other symp-

7. von Hess, C.: Refraction und Akkommodation des menschlichen Auges and ihre Anomalien, in Saemisch, L.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, W. Engelmann, 1910, chap. 12.

8. Erggelet, H.: Ein Beitrag zur Frage der Aniseometropie. Methodischexperimentelle Betrachtung, Ztschr. f. Sinnesphysiol. **49**:326-364, 1916.

9. Tschermak, A.: Optischer Raumsinn, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie mit Berücksichtigung der experimentellen Pharmakologie, Berlin, Julius Springer, 1929, vol. 12.

10. Ogle, K. N.: An Analytical Treatment of the Longitudinal Horopter: Its Measurement and Application to Related Phenomena, Especially to the Relative Size and Shape of the Ocular Images, J. Optic Soc. America **22**:665-728 (Dec.) 1932.

toms of eyestrain, in spite of wearing spectacle lenses which in the judgment of their ophthalmologists are adequate for their needs.

In the preliminary examination of these patients any organic disease of the refractive media or the sensory mechanism of the eye was ruled out by the usual examining methods. The refractive errors were determined usually during homatropine cycloplegia, but occasionally during atropine cycloplegia. The state of balance of the extraocular muscles was determined for both distant and near vision, not only in the primary position but in the various secondary positions of gaze. A Maddox cross and red glass were preferred for this examination. The fusional amplitude for both distant and near vision in both the horizontal and the vertical meridian was measured with rotary prisms. The near point of convergence and the amplitude of accommodation were also measured. Many of the patients were subjected to monocular occlusion of each eye for at least forty-eight hours, and any latent muscle imbalance for the primary position and the secondary directions of gaze was measured.

The results of these examinations being known, the patient was placed at the eikonometer. The power lenses and prisms necessary to correct the refractive errors and muscle imbalances adequately were placed in their proper cells in the instrument. The examiner was then ready to begin the determination of the amount and kind of aniseikonia present.

There are three types of aniseikonia which can be measured with the eikonometer. The first is the over-all size difference, i. e., that in which the ocular image of one eye is symmetrically larger or smaller than the ocular image of the other. The second type is the meridional size difference, that is, that in which the two ocular images are the same size in one meridian but of unequal size in all other meridians. The third type is a combination of over-all and meridional size difference. Most of the work on aniseikonia so far has been to determine the size difference in the 90 and 180 degree meridians. It is possible that meridional aniseikonia at oblique axes may exist in some cases, but a satisfactory clinical method has not yet been developed to determine the axis of oblique meridional aniseikonia. This limitation probably accounts for failures in some cases.

The eikonometer consists of an adjustable head rest with suitable lens cells to hold power lenses and prisms of known surface curves at a known distance from the corneal apex, with a second set of cells to hold the variable over-all and meridional size units. There are also a projection apparatus and screen. Polaroid plates which polarize the light in directions at 90 degrees to each other are placed before each eye, as a partly polarized target is seen on the screen. The portion of this target which is not polarized is visible to each eye. One line of each pair of the four pairs of measuring lines of the target is seen by the right eye. The other line of the pair is seen by the left eye. Each pair of lines is at an equal distance from the center of the target, and each component of the pair is polarized at 90 degrees to the other component of the pair.

The theory of measurement of aniseikonia with the eikonometer is simple, merely a comparison of the relative distance of each member of a pair of lines from the center of the target. However, in the actual performance of the test it may be difficult to obtain this comparison. Usually the first examination is not of much value except to train the patient in observation, for the patient becomes fatigued to the point where his judgment is poor before he is sufficiently adept in making accurate comparisons. As in the measurement of heterophorias one has to consider the so-called amplitude of the fusional movements, so in the measurement of aniseikonia one has to consider the so-called aniseikonic sensitivity, i. e., the range of magnification in which the images appear the same

size. In some cases this may be relatively large, so that only an approximate measurement of the difference in size of the images is possible. After the approximate aniseikonic correction has been used for a time, such a range generally narrows, so that a more accurate determination of the amount of aniseikonia is possible. The measurement of aniseikonia is entirely subjective and requires close attention on the part of the patient. Common difficulties encountered in making the examination, which are troublesome and occasionally make the determination impossible, are poor peripheral fusion, suppression and uncertainty in observation.

Of the first 200 patients who were examined for aniseikonia and who were not suffering from any definite organic ocular or constitutional disease, 86 were found to have a degree of aniseikonia which might be expected to produce symptoms. I have not found any person with less than a 1 per cent size difference who received relief from correction of his aniseikonia, and I feel that the chances of success are much greater if the amount of aniseikonia is 1.50 per cent or more. (The Dartmouth group have records of an occasional patient who received relief of symptoms from correction of a size difference as small as 0.50 per cent.) The maximum amount of aniseikonia compatible with single binocular vision is about 5 per cent. The sensitivity of the patient in recognizing size differences is variable, but for an average person with 20/20 vision in both eyes and good binocular vision it is in the magnitude of 0.25 per cent.

Of the 86 patients in whom 1 per cent or more of size difference was found, 39 reported a lessening or complete relief of symptoms while wearing temporary lenses with the necessary size correction added by means of a hook front. At the time of writing there are 31 patients still wearing temporary glasses, some of whom will get permanent glasses later. Permanent iseikonic lenses were prescribed only for those persons who reported relief of symptoms from wearing temporary glasses. (Two exceptions are reported hereafter.) Of 41 persons for whom permanent glasses were ordered, 3 have reported that they have discontinued the used of their iseikonic glasses. Two of these showed less than 1 per cent difference in size, and permanent glasses were ordered without trial of a temporary correction.

Eikonometric examinations were repeated until a fair degree of consistency in the determined amount of aniseikonia was obtained. This might require only three or four examinations or many trials.

From the results of examination, one can roughly divide persons who show aniseikonia into three groups. The first and largest group is made up of those whose refraction is about equal in the two eyes and whose aniseikonia is essentially the same for both distant and near vision. The second group is made up of those who have considerable anisometropia, the correction of which produces symptoms which are relieved by correction of the associated aniseikonia. The third group is made up of persons who show a relatively low degree of aniseikonia for distant vision but a high degree of meridional aniseikonia at the 180 degree meridian at the near point. In my series of 41 patients for whom permanent glasses were ordered, 28 were classified in group 1, 6 in group 2 and 7 in group 3.

REPORT OF CASES

As there is considerable similarity in many cases, I have chosen a few typical ones representing each group and will report them in detail.

CASE 1.—G. A. D., a man aged 38, a marine engineer, had started visiting ophthalmologists and optometrists at the age of about 15 because of poor vision. He had had many pairs of glasses, all of which improved his vision, but the better his vision the more fatigued his eyes

became. As a result, he seldom wore his glasses. It was almost impossible for him to read the newspaper, because of his poor visual acuity. He carried a small magnifying glass, which he used for reading small print. Besides ocular fatigue, frontal and occipital headaches developed when he wore his glasses. He also suffered from periodic attacks of pain starting in the eyeballs and radiating to the frontal and occipital regions and frequently into the teeth. These attacks were often associated with nausea and vomiting. Repeated medical examinations failed to reveal any organic disease.

Examination showed vision in each eye to be 20/200 (with glasses 20/20). The lids, conjunctiva, sclera, anterior chamber and iris were normal in each eye. The pupils were equal and regular and reacted normally to physiologic stimulation. The lenses and media were clear. The fundi were normal, as were the fields of vision and the blindspots. Refraction with homatropine cycloplegia gave the following results:

Right eye: —0.37 D. sph. ⌒ +2.25 D. cyl., axis 90, vision 20/20
Left eye: —0.75 D. sph. ⌒ +3.00 D. cyl., axis 80, vision 20/20

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	1△ esophoria	6△	24△	3△	3△
Near vision:	6△ esophoria	24△	30△		

The near point of convergence was 85 mm. and the range of accommodation 7.00 D. The prescription recommended was:

Right eye: —0.50 D. sph. ⌒ +2.00 D. cyl., axis 90 (vision 20/20)
Left eye: —1.00 D. sph. ⌒ +2.75 D. cyl., axis 80 (vision 20/20)

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	0.75	90	1.00	90	0.75	90
Left eye	0.75	180	1.00	180	1.00	180
Sensitivity	± 0.25%		± 0.25%		± 025%	
Near vision						
Right eye	...	...	1.75	90	0.25	90
Left eye	1.50	180	1.25	180	1.50	180
	± 0.25%		± 0.25%		± 0.25%	

The following permanent correction was prescribed:

Right eye: —0.50 D. sph. ⌒ +2.00 D. cyl., axis 90 ⌒ 0.75% meridional magnification, axis 90 (vision 20/20)
Left eye: —1.00 D. sph. ⌒ +2.75 D. cyl., axis 80 ⌒ 1.00% meridional magnification, axis 180 (vision 20/20)

The patient has worn his glasses continuously for the past year. He has no more ocular fatigue and is able to read with comfort. He still has an occasional attack of headache associated with nausea and vomiting.

Comment.—This is a typical case of moderate aniseikonia, relatively high mixed astigmatism and slight anisometropia. The patient was an exceptionally good observer, as is shown by the consistency and sensitivity of the results of examination with the eikonometer. The result of the correcting of his aniseikonia as well as his refractive errors has been most gratifying.

CASE 2.—C. S. O., a man aged 36, a minister, complained that he could not read without effort and that he frequently closed his right eye while reading. He began to have trouble with his eyes while in college. He had the feeling that he had to focus on every word, which made reading hard work. His eyes were sensitive to light, and his eyelids were frequently red. The latter symptoms had been helped by the taking of large amounts of vitamin A. He had suffered occasionally from frontal headaches, but they had not been related to the use of the eyes. He had been wearing a vertical prism to correct a hyperphoria and a + 1.00 D. sph. addition for close work to correct a weakened accommodation.

Examination showed vision in the right eye to be 20/30 (with glasses 20/20) and in the left eye 20/40 (with glasses 20/20). The lid margins and conjunctiva were red and congested. The scleras, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic stimulation. The lenses and media were clear. The fields of vision and blindspots were normal. Refraction with homatropine cycloplegia gave the following results:

Right eye: +0.50 D. sph. ⌒ +0.25 D. cyl., axis 10, vision 20/20
Left eye: −0.25 D. sph. ⌒ +1.12 D. cyl., axis 75, vision 20/20

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	− Vertical Divergence
Distant vision:	1△ esophoria	6△	18△	5△	−2△
	4△ right hyperphoria				
	−4° cyclophoria				
Near vision:	6△ exophoria	15△	14△		
	4△ right hyperphoria				

The vertical deviation increased to 6 prism diopters when the patient looked up and decreased to 2 prism diopters when he looked down. The lateral rotation of the eyes in the horizontal plane did not change the amount of hyperphoria. Inclination of the head to either the right or the left shoulder did not alter the hyperphoria. The near point of convergence was 90 mm., and the range of accommodation was 3.50 D. The prescription recommended was:

Right eye: +0.25 D. sph. ⌒ +0.25 D. cyl., axis 10 ⌒ 2△ base down
Left eye: −0.50 D. sph. ⌒ +1.00 D. cyl., axis 75 ⌒ 2△ base up
+1.00 D. sph. addition

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	1.25	90	1.50	90	1.00	90
Left eye	0.25	180	0.25	180	0.25	180
Sensitivity	± 0.25%		± 0.25%		± 0.25%	
Near vision						
Right eye	1.75	90	1.25	90	1.25	90
Left eye	1.00	180	0.50	180	0.75	180
Sensitivity	± 0.50%		± 0.50%		± 0.50%	

The following permanent correction was prescribed:

Right eye: +0.25 D. sph. ⌒ +0.25 D. cyl., axis 10 ⌒ 2△ base down ⌒ 1.00% meridional magnification, axis 90
Left eye: −0.50 D. sph. ⌒ +1.00 D. cyl., axis 75 ⌒ 2△ base up ⌒ 0.25% meridional magnification, axis 180
+1.00 D. sph. addition

The patient had been wearing iseikonic glasses for nine months when last seen. He was well pleased and found reading much easier.

Comment.—This patient had a very complicated ocular apparatus. Many combinations of size correction, vertical prisms and power lenses, with and without reading additions, were tried. The patient showed no signs of a psychoneurosis. He was an extremely sensitive person as far as his eyes were concerned. He could tolerate only the slightest variation from the correction prescribed with respect to power, prism or magnification. It took five months to work out the prescription.

There is probably some relationship between aniseikonia and reading difficulties. Bielschowsky reported the case of the president of a large corporation who showed a spectacular increase in his reading speed after the correction of his aniseikonia. Professor Dearborn, of Harvard, found a high incidence of

aniseikonia among a relatively large group of children with reading difficulties. However, one should not conclude from this that aniseikonia is the sole cause of slow reading. Dr. Imus in his survey of the class of 1940 at Dartmouth College did not find that those students who showed an aniseikonia of 1 per cent or more were poorer readers or poorer students than those without any or with only a low degree of aniseikonia. However, he did find that aniseikonia when present was more likely to produce fatigue in reading, headaches and car, train and sea sickness than was the presence of either refractive errors or motor anomalies.

CASE 3.—Mrs. J. S. C., a woman aged 46, a housewife, complained that her eyes felt strained. She had worn glasses since the age of 5 years, and her vision had always been subnormal. Her eyes had always been sensitive to light, and she had never been able to drive an automobile because of her inability to judge distance. The use of the eyes for close work or moving pictures had frequently precipitated a sick headache.

Examination showed vision in the right eye to be 20/200 (with glasses 20/30) and in the left eye 20/400 (with glasses 20/40). The lids, conjunctivas, scleras, corneas, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic stimulation. The lenses and media were clear. With regard to the fundi, there was a white patch partly overlying the disk and extending about 2 disk diameters from it which was interpreted as a congenital anomaly. There was connective tissue on the left disk, which suggests that the patient may have suffered from optic neuritis in the past. A check on the fields of vision showed that there was a small depression in the upper temporal visual field on the right side and that the blindspot was of normal size. The peripheral visual field and blindspot of the left eye were normal. The intraocular tension was not elevated. Refraction with homatropine cycloplegia gave the following results:

Right eye: + 1.25 D. sph. ⌒ + 2.75 D. cyl., axis 25, vision 20/25
Left eye: + 2.50 D. sph. ⌒ + 2.50 D. cyl., axis 90, vision 20/40

Examination of the intraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	3△ exophoria	10△	10△	6△	5△
Near vision:	14△ exophoria	24△	2△		

The near point of convergence was 150 mm. and the range of accommodation 5.00 D. The prescription recommended was:

Right eye: + 1.00 D. sph. ⌒ + 2.75 D. cyl., axis 25 ⌒ 2△ base in (vision 20/20)
Left eye: + 2.25 D. sph. ⌒ + 2.50 D. cyl., axis 90 ⌒ 2△ base in (vision 20/30)

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	3.00	90	3.50	90	3.00	90
Left eye	...	..	0.75	180	1.50	180
Sensitivity	± 0.50%		± 0.50%		± 0.50%	
Near vision						
Right eye	2.50	90	4.00	90	3.50	90
Left eye	0.50	180	1.25	180	1.75	180
Sensitivity	± 1.00%		± 1.00%		± 0.75%	

The following permanent correction was prescribed:

Right eye: + 1.00 D. sph. ⌒ + 2.75 D. cyl., axis 25 ⌒ 2△ base in ⌒ 3.25% meridional magnification, axis 90
Left eye: + 2.25 D. sph. ⌒ + 2.50 D. cyl., axis 90 ⌒ 2△ base in ⌒ 1.50% meridional magnification, axis 180

The patient reported that she had been wearing her glasses with comfort and that she had much less photophobia. She had been able to drive her automobile.

Comment.—This patient was difficult to examine with the eikonometer because of the unequal visual acuity in the two eyes and the tendency to suppress the image of the left eye. She had a high refractive error and poor convergence but an abnormal amount of accommodation for her age. She had a moderate amount of anisometropia. The degree of aniseikonia present approached the upper limit compatible with single binocular vision and might have been the cause of her suppression, amblyopia, exophoria and poor judgment of distance. Her first comment on returning to the office with her temporary glasses was: "I never realized Market Street was so far away." She could appreciate depth perception of a degree which she had not realized before. It has not been my experience that I could neglect heterophoria or that there was a change in the heterophoria after the correction of aniseikonia, as has been claimed by some workers.

CASE 4.—S. W. C., a woman aged 49, a housewife, suffered from pain in the eyes and forehead. She had worn glasses since the age of about 12. She had been forced to stop school in her second year of high school because of her inability to use her eyes for close work. She had not read a book, magazine or newspaper in ten years. She had worn dark glasses when outside for the past fifteen years and had suffered excessively from photophobia. A pain in the eyes and a frontal headache would develop whenever she attempted to use her eyes. She had been able to tolerate only about twenty to forty-five minutes of a motion picture without symptoms. She had been forced to keep her eyes closed when riding in an automobile or train in order to prevent car or train sickness. She had had many general medical and ophthalmologic examinations, none of which disclosed any organic disease. She had tried many pairs of glasses, but the more acute her vision, the more severe her symptoms.

Examination showed vision in the right eye to be 20/400 (with glasses 20/40) and in the left 20/400 (with glasses 20/40). The lid margins were red and swollen and the conjunctivas congested. The scleras and corneas were normal. The anterior chambers were shallow. The pupils were regular and equal and reacted normally to physiologic stimulation. The lenses and media were clear. The fundi, the fields of vision and the blindspots were normal. The intraocular tension was not elevated. Refraction with homatropine cycloplegia gave the following results:

Right eye: + 4.00 D. sph. ⌒ + 1.62 D. cyl., axis 100, vision 20/25
Left eye: + 3.00 D. sph. ⌒ + 1.00 D. cyl., axis 80, vision 20/25

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	orthophoria	5△	18△	4△	5△
Near vision:	2△ exophoria	24△	22△		

There was 1 prism diopter of right hyperphoria after occlusion of the right eye for forty-eight hours, while when the left eye was occluded for forty-eight hours 2½ D. of left hyperphoria developed. The near point of convergence was 110 mm. and the range of accommodation 2.00 D.

The prescription recommended was:

Right eye: + 3.75 D. sph. ⌒ + 1.50 D. cyl., axis 100 ⌒ ¾△ base up
Left eye: + 3.25 D. sph. ⌒ + 1.00 D. cyl., axis 80

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	0.50	180	0.50	180	0.50	180
Left eye	1.25	90	0.75	90	1.00	90
Sensitivity	± 0.25%		± 25%		± 0.25%	

The following permanent correction was prescribed:

Right eye: + 3.75 D. sph. ⊃ + 1.50 D. cyl., axis 100 ⊃ ¾△ base up ⊃ 0.50% meridional magnification, axis 180

Left eye: + 3.25 D. sph. ⊃ + 1.00 D. cyl., axis 80 ⊃ 1.00% meridional magnification, axis 90

This patient's first iseikonic glasses were prescribed about four months before the time of writing, and she is still under observation.

Comment.—My first impression of this patient was that she was suffering from a psychoneurosis. It was necessary to do most of my examinations in a dark room, and it was impossible to use a retinoscope or an ophthalmoscope until recently because of the extreme photophobia. She was an excellent observer, as is shown by the consistency and sensitivity of the results of eikonometric examination. She was given her prescription made in white glass. The change that had occurred after she had worn her aniseikonic correction for one month was remarkable. She had practically discarded her dark glasses. She was no longer car sick from riding in either an automobile or a train. Her disposition was much improved, and her whole outlook on life had changed. I have a patient whose case is somewhat similar who had a recurrence of the nervous symptoms when by mistake the right lens was placed before the left eye and vice versa when the frames of her glasses were changed. The lenses were identical except for the magnification factor. When the lenses were correctly placed in her frames, her symptoms subsided.

A reduction in photophobia such as that which occurred in this case is common after the correction of aniseikonia.

As mentioned before, corrected anisometropia is often associated with aniseikonia, but the importance of anisometropia as a basis of aniseikonia has been overemphasized. The amount of aniseikonia found in cases of corrected anisometropia has frequently been shown to differ markedly from that which might be expected from mathematical computations. It must be borne in mind that it is only the correction of anisometropia which is due to a difference in the power of the dioptric apparatus of the eyes which produces aniseikonia, while correction of anisometropia which is caused by a difference in length of the axes of the eyes does not produce aniseikonia if the lenses are placed at the anterior focal point of the eyes. Any size difference due to the correction of the anisometropia may increase, decrease or compensate for existing aniseikonia. This might explain the tolerance of some persons to the correction of relatively high degrees of anisometropia or the intolerance of other persons to the correction of relatively low degrees of anisometropia. The visual act in anisometropia is most complicated and should be investigated in the light of newer developments.

With these facts in mind, I should like to report 2 cases of a moderate amount of anisometropia in which the patient was helped by the addition of a size correction to the lenses. Incidentally, I have case records of a number of patients with large amounts of anisometropia who by the usual tests for single binocular vision are using the two eyes together, who show an equal or greater amount of measurable aniseikonia than is shown by these 2 patients and who do not suffer from any asthenopic symptoms.

CASE 5.—Lieutenant A. W. T. G., aged 58, a physician in the United States Navy, had had headaches and nervous exhaustion after close work for thirty years. He had had repeated medical, neurologic, psychiatric, laboratory, otologic, and ophthalmologic examinations by civilian and service physicians in various parts of the United States. His symptoms had been severe for the past ten years, making it necessary for him to retire from active duty.

Examination showed vision in the right eye to be 20/400 (with glasses 20/200) and in the left eye 20/100 (with glasses 20/25). The lids, conjunctivas, scleras, corneas, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic

stimulation. The lenses and media were clear. The fundi were normal except for moderate retinal arteriosclerosis. The fields of vision and blindspots were normal. The intraocular tension was not elevated. Refraction with homatropine cycloplegia gave the following results:

Right eye: + 4.00 D. sph. ⌒ + 1.25 D. cyl., axis 70, vision 20/40
Left eye: + 1.50 D. sph. ⌒ + 1.00 D. cyl., axis 65, vision 20/20

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	2△ exophoria	6△	16△	4△	4△
Near vision:	14△ exophoria	20△	8△		

The near point of convergence was 250 mm., and the range of accommodation was 1.00 D. The prescription recommended was:

Right eye: + 4.00 D. sph. ⌒ + 1.25 D. cyl., axis 105 (vision 20/40)
Left eye: + 1.50 D. sph. ⌒ + 1.00 D. cyl., axis 65 (vision 20/20)
+ 2.25 D. cyl. addition

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Magnification	2d Examination Magnification	3d Examination Magnification
Distant vision			
Right eye:	.....	.....	.....
Left eye:	2.75% over-all ⌒ 2.25% meridional, axis 90	3.5% over-all ⌒ 1.75% meridional, axis 90	4.0% over-all ⌒ 1.5% meridional, axis 90
Sensitivity	± 1.00%	± 0.50%	± 0.50%
Near vision			
Right eye:	3.0% over-all ⌒ 2.5% meridional, axis 90	3.75% over-all ⌒ 3.0% meridional, axis 90	4.0% over-all ⌒ 3.5% meridional, axis 90
Sensitivity	± 1.50%	± 1.00%	± 1.00%

The following permanent correction was prescribed:

Right eye: + 4.00 D. sph. ⌒ + 1.25 D. cyl., axis 105
Left eye: +1.50 D. sph. ⌒ + 1.00 D. cyl., axis 65 ⌒ 3.50% over-all magnification

The patient at the time of writing has been wearing his iseikonic lenses for one year. He can now do close work without headaches. His nervousness is much improved, and he has gone back to active duty in the medical department of the Navy.

Comment.—This case represents a moderately high degree of anisometropia and a very high degree of aniseikonia. The patient had a rather marked weakness of convergence and theoretically would have been helped by the use of prisms, base in, for close work. However, it is not possible to grind segments of prism base in in eikonic bifocal lenses. He was advised that it might be necessary for him to use a separate pair of reading glasses with the prismatic correction to compensate for his weakness in convergence. Fortunately this has been found unnecessary.

The patient has had considerable trouble keeping his glasses properly adjusted because of pronounced facial asymmetry. It is necessary that the distance from the apex of the cornea to the center of the eye wire of the glasses be exact, as the magnifying power of the lenses is a function of the distance. In this case, in which there is a strong lens before the right eye and a moderately strong lens before the left eye, the change in magnifying power induced by moving the right lens away from the cornea 1 mm. and keeping the left lens fixed is about 0.50 per cent. The patient has had to make two trips back to San Francisco to have his glasses adjusted, because when they were inadequately adjusted elsewhere there was a recurrence of his symptoms. The problem of keeping his glasses, as well as those of many other patients, adjusted has been trying

at times, especially when one has had to depend on opticians not acquainted with, and occasionally at the same time antagonistic to, the principiles of aniseikonia.

CASE 6.—J. C., a schoolgirl aged 19, had had headaches for the past year. She gave a history of having worn glasses for several years to correct her nearsightedness. She had frequently had trouble with headaches when her glasses were too strong. About one year before, she began having headaches which she described as a pressure feeling all over her scalp. She had suffered periodic attacks of severe and one-sided headaches associated with nausea and vomiting. She had had thorough medical examinations and several changes in glasses, none of which relieved her of her symptoms.

Examination showed vision in each eye to be 20/400 (with glasses 20/20—). The lids, conjunctivas, scleras, corneas, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic stimulation. The fundi, the peripheral fields of vision and the blindspots were normal. Refraction with atropine cycloplegia gave the following results:

Right eye: —5.50 D. sph. ⌒ +2.00 D. cyl., axis 30, vision 20/20
Left eye: —3.50 D. sph. ⌒ +1.25 D. cyl., axis 90, vision 20/20

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	1△ right hyperphoria	8△	28△	5△	2△
Near vision:	4△ esophoria				
	1△ right hyperphoria	28△	24△		

Examination of the extraocular muscles after occlusion of the right eye for seventy-two hours showed 4 prism diopters of exophoria and 2.5 prism diopters of right hyperphoria, while after occlusion of the left eye for seventy-two hours there was 3 prism diopters of exophoria with vertical orthophoria.

The near point of convergence was 90 mm. and the range of accommodation 10.00 D. The prescription recommended was:

Right eye: —5.50 D. sph. ⌒ +2.00 D. cyl., axis 30
Left eye: —3.50 D. sph. ⌒ +1.25 D. cyl., axis 90 ⌒ 1½△ base up

This patient was the most difficult to examine of any seen to date. In spite of the fact that she showed a fair degree of sensitivity at any one examination, it was impossible to repeat the examination and check the results of a previous test. There had always been a tendency to find that in the right eye the image in the 180 degree meridian was smaller and that in the 90 degree meridian possibly larger than those in the corresponding meridians in the left eye. After doing fifteen eikonometric examinations, I decided to try to find out whether the patient was sensitive to size lenses and, if so, what was the upper limit of tolerance. Meridional size lenses, axis 90, were placed in front of the right eye beginning with a 1.0 per cent magnification, and at about weekly intervals the magnification was increased by a 0.50 per cent. No effect of the size lens was noted until a 2.50 per cent meridional magnification, axis 90, was placed before the right eye. This seemed to make the patient a little more comfortable, which was encouraging, but she had experienced temporary decreases in symptoms without cause in the past. The trial and error method was continued. A 3.0 per cent meridional magnification, axis, 90, before the right eye was tried, and this seemed to be satisfactory. A 0.50 per cent meridional magnification, axis 180, was placed before the left eye in addition to the 3.0 per cent meridional magnification, axis 90, before the right eye. This combination was also well tolerated, and the headaches became less severe. She was able to do some reading. The meridional magnification, axis 90, before the right eye was increased to 4.0 per cent, and the 0.5 per cent meridional magnification, axis 180, allowed to remain before the left eye. This combination was above the limit of tolerance. After wearing it for a few hours the patient experienced a severe headache associated with nausea and vomiting, and the symptoms lasted six days in spite of the fact that the size correction was reduced. As soon as she was feeling better again, the combination was tried once more, with the same disastrous results. After about six months the following permanent prescription for eikonic lenses was ordered:

Right eye: —5.50 D. sph. ⌒ +2.00 D. cyl., axis 30 ⌒ 3.0% meridional magnification, axis 90
Left eye: —3.50 D. sph. ⌒ +1.25 D. cyl., axis 90 ⌒ 1½△ base up

These glasses were satisfactory until Dec. 7, 1942, when the Japanese attacked Pearl Harbor and the Philippines, after which there was a recurrence of symptoms. Fortunately, however, this was only temporary; the symptoms subsided after one month and the patient is now comfortable and is employed doing clerical work.

Comment.—This case represents a very sensitive nervous system with what might be called a headache constitution. Such a constitution was brought out in the history by the statement that the patient had frequently experienced headaches from new glasses because they were too strong and by her psychologic upset following the attack on the United States.

The next group of cases are those of patients who were relatively comfortable as long as they did not use their eyes for close work, and examinations with the eikonometer showed only the smallest degree of aniseikonia for distant vision but a fairly large amount of meridional size difference in the 180 degree meridian at the near point.

CASE 7.—S. L. G., a man aged 25, a saddle maker, complained that his eyes tired on close work. He had suffered from ocular fatigue, pain in his eyes and headaches, often associated with nausea and vomiting, for the past ten years. These symptoms always followed prolonged close work. He had tried glasses of various powers and prism strengths in all directions without relief. He had also taken many orthoptic treatments but without increasing his ability to do close work.

Examination showed vision in each eye to be 20/20. The lids, conjunctivas, corneas, scleras, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic stimulation. The fields of vision and fundi were normal. Refraction with homatropine cycloplegia gave the following results:

Right eye: + 0.37 D. sph. ⌒ + 0.25 D. cyl., axis 90, vision 20/20
Left eye: + 0.50 D. sph. + 0.37 D. cyl., axis 75, vision 20/20

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+ Vertical Divergence	— Vertical Divergence
Distant vision:	orthophoria	6△	18△	3△	3△
Near vision:	3△ exophoria	20△	20△		

The near point of convergence was 85 mm. and the range of accommodation 11.00 D. The prescription recommended was:

Right eye: 0.25 D. cyl., axis 90
Left eye: + 0.25 D. sph. ⌒ + 0.37 D. cyl., axis 75

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	0.25 (⌒ 0.25% over-all)	90	0.50	90	0.25	90
Left eye	...	...	...	...	...	...
Sensitivity	± 0.25%		± 0.25%		± 0.25%	
Near vision						
Right eye	4.00	90	2.50	90	2.75	90
Left eye	...	...	...	...	...	...
Sensitivity	± 1.50%		± 1.00%		± 1.00%	

The following permanent correction was prescribed for close work:

Right eye: + 0.25 D. cyl., axis 90 ⌒ 2.75% meridional magnification, axis 90
Left eye: + 0.25 D. sph. ⌒ + 0.37 D. cyl., axis 75

These eikonic glasses have been in use for about one year and have caused a marked relief of symptoms. The patient no longer becomes fatigued from close work, and he seldom has a headache.

CASE 8.—F. B. H., a man aged 25, a draftsman, complained of ocular fatigue and aching of the eyeballs from close work. He was moderately myopic and had worn glasses for several years. He had always worn a slight undercorrection because he had found this more comfortable than a full correction. His symptoms had become worse in the past two years, during which time he had had six changes of glasses.

Examination showed vision in each eye to be 20/100 (with glasses 20/25). The lid margins and conjunctivas were red and congested. The corneas, scleras, anterior chambers and irises were normal. The pupils were equal and regular and reacted normally to physiologic stimulation. The fundi and fields of vision were normal. Refraction with homatropine cycloplegia gave the following results:

Right eye: —1.25 D. sph. ⌒ +0.62 D. cyl., axis 175, vision, 1.0
Left eye: —2.00 D. sph. ⌒ +0.25 D. cyl., axis 120, vision, 1.0

Examination of the extraocular muscles gave the following results:

	Balance	Prism Divergence	Prism Convergence	+Vertical Divergence	—Vertical Divergence
Distant vision:	orthophoria	6△	16△	3△	3△
Near vision:	orthophoria	24△	24△		

The near point of convergence was 70 mm., and the range of accommodation was 10.00 D. The prescription recommended was:

Right eye: —1.00 D. sph. ⌒ +0.50 D. cyl., axis 175 (vision, 1.0)
Left eye: —1.75 D. sph. ⌒ +0.25 D. cyl., axis 120 (vision, 1.0)

The results of examination with the eikonometer through the recommended prescription were as follows:

	1st Examination Meridional Magnification		2d Examination Meridional Magnification		3d Examination Meridional Magnification	
	Percentage	Axis	Percentage	Axis	Percentage	Axis
Distant vision						
Right eye	...	...	...	...	...	...
Left eye	0.75	180	0.50	180	0.50	180
Sensitivity	±0.25%		±0.25%		±0.25%	
Near vision						
Right eye	...	...	...	...	...	...
Left eye	2.5 (⌒ 0.50% over-all)	90	1.50	90	2.00	90
Sensitivity	±1.00%		±1.00%		±0.75%	

The following permanent correction was prescribed:

Right eye: —1.00 D. sph. ⌒ +0.50 D. cyl., axis 175
Left eye: —1.75 D. sph. ⌒ +0.25 D. cyl., axis 120 ⌒ 2.00% meridional magnification, axis 90

These glasses were worn with marked relief of symptoms for about six months. Then there was a recurrence of ocular fatigue and pain in the eyeballs. The aniseikonia was checked again, and it was found that it had changed to 3.25 per cent meridional magnification, axis 90, before the left eye. This correction was used in a temporary frame with a hook front and relieved the fatigue for about two months, after which there was an exacerbation of the symptoms. The patient returned to his original glasses and found that they were again comfortable. Examination with the eikonometer at this time showed the aniseikonia to be 2.0 per cent meridional magnification, axis 90, not 3.25 per cent meridional magnification, axis 90. My last report from the patient was that he was working forty-eight hours per week as a draftsman and reading three to four hours at night without symptoms.

Comment.—The last 2 cases may represent what might be called latent aniseikonia. It has been found by long and detailed examinations of persons who show aniseikonia for near and very little for distant vision that if for a few days they wear a size lens somewhere between the one found correct for distance and that found correct at the near point it is possible to unmask a degree of aniseikonia for distant vision which is not present under ordinary conditions. In cases 7 and 8, eikonometric examinations for distant vision after the patient had worn eikonic glasses for near vision for a few months showed greater aniseikonia than that found at the original examination. Only time will reveal whether patients such as the ones in these 2 cases will need iseikonic glasses for distant vision in the future.

CONCLUSION

In this short discussion I have tried to outline the development of the work on aniseikonia and point out a few of the problems which are still unsolved. Aniseikonia does not exist in every patient who suffers from fatigue on reading; headaches; car, train and sea sickness, or other asthenopic symptoms which are not relieved by correction of the refractive errors or muscle imbalance or both. From clinical experience I have found that only about 1 of 5 patients suffering from such symptoms can be relieved by correction of aniseikonia.

Of the 16 patients who tried temporary corrections for aniseikonia and experienced no relief of symptoms, only 4 had 1.5 per cent or more of aniseikonia.

An aniseikonia of 1.5 per cent does not occur frequently in the average run of patients. In a series of 100 patients who were relieved of their symptoms by adequate correction of their refractive errors, I did not find any person with this amount of aniseikonia. In a series of 280 aviation cadets at Pensacola, Fla., it was found that only 85 per cent had as much as 0.50 per cent of aniseikonia and none were found with 1.0 per cent or more of aniseikonia. I recognize that these are too few series to provide the basis for a general statement, but the figures do seem to indicate that an aniseikonia of 1.5 per cent is not common in patients without symptoms, and, as stated before, that of persons suffering from symptoms of eyestrain and having 1.5 per cent of aniseikonia, one can expect the symptoms to be abated in a fair percentage after correction of the aniseikonia.

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RUPTURE OF ANEURYSM OF CIRCLE OF WILLIS

RELATIONSHIP BETWEEN INTRAOCULAR AND INTRACRANIAL HEMORRHAGE

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The earliest account of intraocular hemorrhage associated with intracranial hemorrhage which had extended into the intervaginal spaces of the optic nerve was the observation of Hale-White [1] in 1895. He stated the belief that "the hemorrhage had passed forward in the sheath of the optic nerves which were much distended with blood clot and ultimately tore its way forward under the retina."

Uhthoff [2] was one of the first to question the validity of this belief. Other investigators (Dupuy-Dutemps,[3] Riddoch and Goulden [4] and Macdonald [5]) have shown by histopathologic examination that there was no evidence of blood having traveled from either the subdural or the subarachnoid space around the nerve forward into the eye. Since the publication of their reports, there has been considerable controversy over the relationship between intraocular hemorrhage and intracranial hemorrhage.

According to Fearnsides,[6] the first definite account of an intracranial aneurysm was published by Biumi, of Milan, in 1765. The earliest complete analysis of reported cases was by Sir William Gull [7] in 1859. He observed that these aneurysms commonly occurred in young subjects without general disease of the vessels and were fatal either from rupture of the sac or from pressure or softening around it.

In the opinion of Beadles,[8] it was impossible to diagnose an aneurysm of any one of the cerebral arteries except in the most unusual circumstances. Likewise, Fearnsides agreed with Gull's statement that "although we may from the circumstances sometimes suspect the presence of an intracranial aneurysm, we have at the best no symptoms upon which to ground more than a probable diagnosis."

On the other hand, Symonds [9] in 1923 reported 5 cases in which the diagnosis of intracranial aneurysm was made before death, and he concluded that "the conjunction of the history of such an attack of basal meningeal hemorrhage with the signs of a tumor at the base of the brain is sufficient evidence for the diagnosis of intracranial aneurysm." Cushing [10] stated the belief that an aneurysm should always be considered in a differential diagnosis when an apoplectic attack or a series of attacks of comparatively sudden onset is followed by symptoms pointing to the region of the internal carotid artery in its intracranial portion, and should there be, in addition, subhyaloid retinal hemorrhages and the cerebrospinal spaces be found to contain free blood, a diagnosis would be reasonably certain.

Read before the New York Academy of Medicine, Section of Ophthalmology, Feb. 15, 1943.

1. Hale-White, W.: Tr. Clin. Soc. London **28**:5, 1895.
2. Uhthoff, W.: Ber. ü. d. Versamml. d. ophth. Gesellsch. **29**:143, 1901.
3. Dupuy-Dutemps, L.: Ann. d'ocul. **151**:161, 1914.
4. Riddoch, G., and Goulden, C.: Brit. J. Ophth. **9**:209, 1925.
5. Macdonald, A. E.: Tr. Am. Ophth. Soc. **29**:418, 1931.
6. Fearnsides, E. G.: Brain **39**:224, 1916.
7. Gull, W.: Guy's Hosp. Rep. **5**:281, 1859.
8. Beadles, C. F.: Brain **30**:285, 1907.
9. Symonds, C. P.: Guy's Hosp. Rep. **72**:139, 1923.
10. Cushing, H.: Guy's Hosp. Rep. **72**:159, 1923.

Geoffrey Jefferson [11] discussed the relationship of the optic nerve, chiasm and optic tract to the circle of Willis and emphasized the importance of determination of the fields and angiography as adjuncts to diagnosis.

PATHOLOGY

Most of the earlier writers (among them Church [12] and Bartholow [13]) were of the opinion that intracranial aneurysms were primarily caused by syphilis or were the result of emboli from vegetative endocarditis. Eppinger [14] said that these aneurysms had a congenital origin and were due to an inborn defect in the elastic properties of the arterial wall. Von Hofmann [15] was the first to observe that the favorite sites are (*a*) the bifurcation of the larger vessels and (*b*) the points of division of their branches.

Turnbull [16] found the pathologic change to be medial degeneration following congenital developmental deficiency. Paton [17] called attention to the fact that the arterial system at the base of the brain is almost unsupported, with no solid tissue to prevent the walls from yielding. This circumstance combined with congenital maldevelopment in the vessels renders the arteries constituting the circle of Willis and its branches particularly prone to aneurysms.

Fearnsides, in discussing the etiology of intracranial aneurysms, concluded that there must be some additional factor and this probably, as Eppinger first suggested, is an inherent weakness due to a congenital abnormality in the structure of the arteries at their points of junction and bifurcation.

More recently, Forbus,[18] in an exhaustive study of miliary aneurysms of the cerebral arteries, found a muscular defect in the media located in the portion of the vessel wall forming the angle of bifurcation. This defect was also present in the coronary and mesenteric arteries. He concluded that the aneurysms are lesions independent of any inflammatory process, arteriosclerosis or external trauma and as such are not congenital malformations. He called them acquired lesions arising from a combination of focal weakness in the vessel wall, resulting from a congenital defect in the muscularis and a degeneration of the internal elastic membrane due to overstretching.

INTRAOCULAR HEMORRHAGE

The earliest account of intraocular hemorrhage associated with intracranial hemorrhage was that of Hale-White. Uhthoff was certain that the intraocular hemorrhage in the case reported by him had not penetrated into the papilla from the vaginal space but resulted from marked venous engorgement. Dupuy-Dutemps, in histopathologic examinations, was unable to determine any relation or continuity between the intraocular hemorrhage and the vaginal hematoma, but stated the belief that the retinal hemorrhages were produced by rupture of small retinal vessels.

Symonds [19] stated:

> The relatively large extravasations of blood seen in the fundus . . . were a striking clinical feature. They appeared to be subretinal and the discovery of semi-coagulated droplets of blood

11. Jefferson, G.: Brain **60**:444, 1937.
12. Church, W. S.: St. Barth. Hosp. Rep. **6**:99, 1870.
13. Bartholow, R.: Am. J. M. Sc. **64**:373, 1872.
14. Eppinger, H.: Arch. f. klin. Chir. **35**:1, 1887.
15. von Hofmann, E.: Wien. klin. Wchnschr. **7**:823, 1894.
16. Turnbull, H. M.: Brain **41**:50, 1918.
17. Paton, L.: Tr. Ophth. Soc. U. Kingdom **44**:110, 1924.
18. Forbus, W. D.: Bull. Johns Hopkins Hosp. **47**:239, 1930.
19. Symonds, C. P.: Quart. J. Med. **18**:93, 1924.

within the arachnoid sheath of the optic nerve, post mortem, suggested that those seen in the fundus had found their way from the general lake of extravasation along this path to the nerve head.

Symonds was of the opinion also that there was sufficient pressure in the optic nerve sheaths to force a passage through the lamina cribrosa.

Paton [20] declared that in a small but definite percentage of cases the retinal hemorrhages are due to direct leakage of blood from the sheath through the lymphatic spaces at the sides of the lamina cribrosa and along the central vessels into the disk head and retinal and preretinal tissues.

Occasionally massive vitreous hemorrhages have been seen, completely obscuring the details of the fundus. In a case reported by Riddoch and Goulden, the subarachnoid space was full of blood. This did not pass into the pial sheath, and no sign of hemorrhage could be found within the nerve or along the vessels within the nerve. They concluded that histologic investigations in this case strongly suggested that the cause of the intraocular hemorrhage in such cases is obstruction of the central vein of the retina at the point where it leaves the optic nerve and enters the dural sheath. The mechanism of the production of hemorrhage would therefore be the same as that for papilledema due to intracranial pressure.

Macdonald reported on a series of 4 cases in which the patient came to necropsy after nontraumatic intracranial hemorrhages. He stated: "Anatomically the cases here reported did not show any direct continuity between the subdural spaces and the intraocular pool of hemorrhage either by way of the perivascular lymph spaces of the central vessels of the optic nerve or at the site of the optic nerve between the lamina cribrosa and the scleral fibers." His conclusions coincided with those of Riddoch and Goulden that the increased intracranial pressure produces congestion of the central vein of the nerve by obstructing the flow of blood as the vein passes through the meningeal spaces and that subhyaloid hemorrhage results from back pressure in the veins of the retina, causing a rupture. He pointed out that the dura about the optic nerve is the only dura not supported by bony walls; hence it distends readily from pressure transmitted along the optic nerve from the corresponding spaces within the cranium.

Unfortunately, in a large percentage of the earlier cases reported fundus examinations were not performed. However, by far the most frequent pathologic observation was papilledema. Wagener and Foster [21] stated that in their experience hemorrhages into the retina had been the most frequent ocular finding and had occurred in a high percentage of their cases, edema of the disk being a much less constant symptom.

REPORT OF A CASE

L. B., a Negro woman aged 48, married and employed as a domestic servant, was admitted to the emergency room of the Central Dispensary and Emergency Hospital on April 5, 1941, in an unconscious condition.

Present Illness.—The patient had complained of occasional headaches about the frontal area for four or five years. They had not been a dominant symptom and would leave after the patient rested. There were no visual disturbances, nausea or vomiting. The day of admission the patient began to have a dull frontal headache which persisted throughout the afternoon. She did not feel particularly well and went walking alone to get some fresh air. She returned home and cooked supper. The headache became slightly worse, and the patient felt somewhat nauseated. She began to wash dishes and suddenly lost consciousness. When she awoke in the emergency room at the hospital, she was able to answer questions coherently and to

20. Paton, L., and Holmes, G.: Tr. Ophth. Soc. U. Kingdom **31**:117, 1911.
21. Wagener, H. P., and Foster, R. F.: Proc. Staff Meet., Mayo Clin. **10**:225, 1935.

understand all conversation. There was no definite localized weakness. Her frontal headache was dull but severe and she noticed gradually increasing nervous tension and tightness in the back of her neck, with pain on bending or twisting her neck. On her arrival in the ward, this became more pronounced.

History.—The past history and the family history were noncontributory.

Physical Examination.—The head, chest, heart and abdomen were normal. Neuromuscular examination gave negative results except to show that the neck was almost rigid. The systolic blood pressure was 118 mm. and the diastolic 60 mm. of mercury.

Spinal puncture on April 5 revealed an initial pressure of 300 mm. of water. The Queckenstedt reaction was negative. The fluid was light wine color and probably contained blood. A sample of 25 cc. was removed and sent to the laboratory for routine examination. The patient continued to complain of frontal headache but otherwise felt well. The neck was becoming rigid. Kernig and Babinski signs were absent. The impression was of subarachnoid hemorrhage.

Course.—On April 12 examination of the fundi showed no abnormalities. The vessels were normal, and there was no choking of the disks or hemorrhage. A sudden onset of severe frontal pain occurred when the patient started to eat about noon. The pain went down the neck and back, and headache persisted. The impression was of recurrent subarachnoid hemorrhage. It was decided that a spinal puncture would be made later if the pain persisted and was severe, the pulse slowed or the patient lost consciousness. The pulse rate was then 80 and regular. The blood pressure was 188 systolic and 100 diastolic. The patient complained of faintness, but there was no loss of consciousness with pain at the onset. The plantar surface of the right foot was numb. The Babinski sign was absent on the left and equivocal on the right.

On April 28 a consultation was held with a neurosurgeon. In the morning the patient suddenly became paralyzed on the left side. At 1 p. m. the paralysis had greatly improved, yet the patient was slightly stuporous. The neck showed stiffness of grade 1. There was slight weakness of the left side of the face; otherwise the muscles were normal. The fundi were normal. The advice was to leave the patient alone and do no more spinal punctures. There had probably been another hemorrhage.

On May 3 the patient suddenly lost consciousness. She flexed both arms occasionally. The right pupil was dilated and the left contracted. Occasionally the patient drew the right side of the face toward the right. The blood pressure was 244 systolic and 128 diastolic. The heart and lungs were normal. The reflexes of the upper extremities were normal. The Babinski sign was present on both sides, with the reflexes more active on the right side than on the left. The neck was fairly stiff.

On May 4 ophthalmoscopic examination, made just prior to death, showed that in the right eye the media were clear and the disk margins mildly indistinct. To the temporal side of the disk was a fairly large preretinal hemorrhage. The veins were engorged; the arteries showed no suggestion of sclerosis. In the left eye the appearance of the disk and vessels was the same as in the right eye. No hemorrhage was seen.

The spinal fluid showed a reaction for globulin of 4 plus and contained blood. Numerous red blood cells were present. The Wassermann reaction was negative. The blood pressure during the patient's stay in the hospital ranged between 140 and 244 mm. of mercury systolic and 60 and 128 mm. diastolic. The respiratory rate remained around 20. The temperature was essentially normal. The pulse rate ranged between 80 and 100.

Summary.—The patient entered the hospital with fairly typical signs of subarachnoid hemorrhage. The presence of this lesion was confirmed by spinal puncture. There were three episodes in twenty-seven days in the hospital, and death occurred.

Diagnosis.—The diagnosis was intracranial aneurysm with rupture and recurrent hemorrhages into the subarachnoid space, bilateral papilledema and subhyaloid hemorrhage in the right eye.

Postmortem Examination.—No abnormality was revealed except the intracranial disease. On removal of the skull cap, a massive subarachnoid hemorrhage of the right side was exposed. After removal of the circle of Willis, examination disclosed an aneurysm about 6 mm. in diameter at the junction of the anterior communicating and the right anterior cerebral artery (fig. 1). The aneurysm was firm and gave the impression that it was thrombosed. The specimen was preserved *in toto* and was injected with colloidal thorium dioxide for roentgen examination. The roof of the right orbit was removed, the optic nerve being exposed. Throughout its orbital portion, the sheath was found to be much dilated and bluish. The nerve was removed from the chiasm down to and including the posterior one half of the globe.

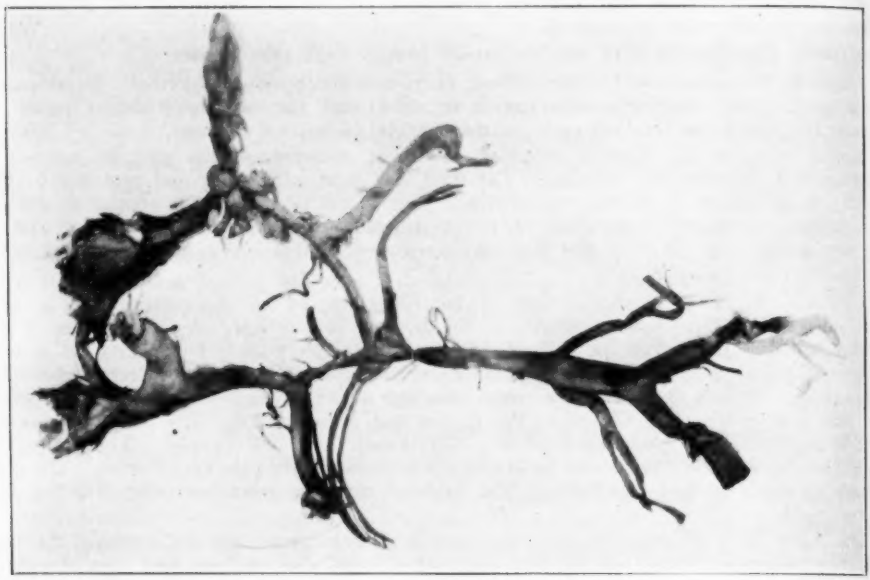

Fig. 1.—The circle of Willis, showing a saccular aneurysm at the junction of the right anterior cerebral and the anterior communicating artery. (Reproduced from United States Army Medical Museum negative 71805.)

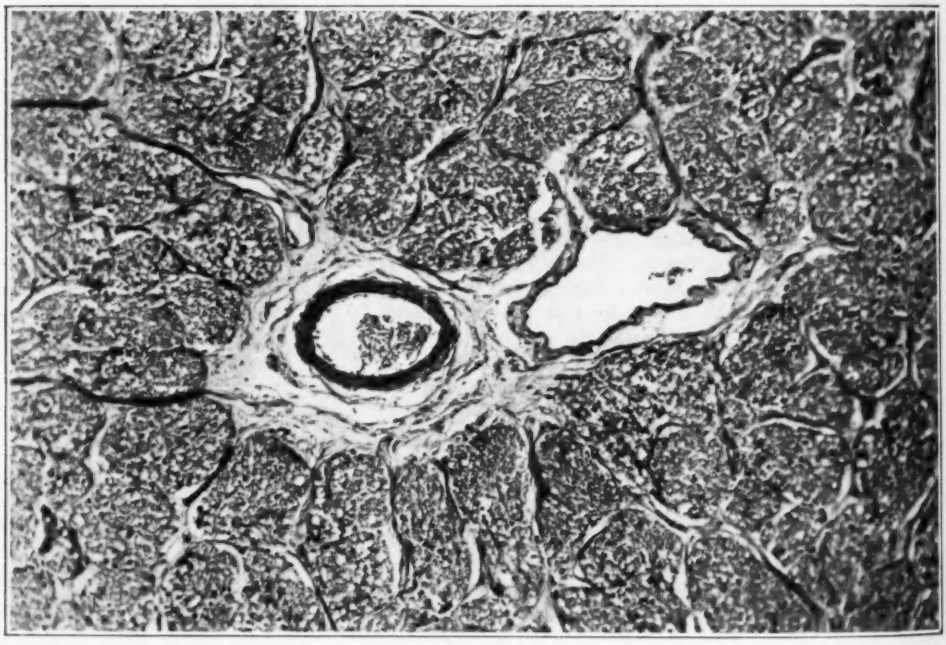

Fig. 2.—Dilatation of the central vein posterior to the lamina cribrosa. (Reproduced from United States Army Medical Museum negative 74346.)

Histopathologic Examination: Serial sections were made of a specimen including the posterior one half of the globe and extending posteriorly to a point behind the entrance of the central vessels into the optic nerve. Microscopic examination revealed hemorrhage, consisting of red blood cells enmeshed in fibrin, in the posterior portion of the vitreous chamber just anterior to the nerve fiber layer in the macular area. The outer plexiform layer of the retina posteriorly and the nerve head were edematous. Within the nerve head the central vein was widely dilated, and both artery and vein were surrounded by an area of marked edema (fig. 2). Behind the lamina cribrosa was an area of edema in the optic nerve; this did not extend to the point of entrance of the central vessels. A narrow band of edema just

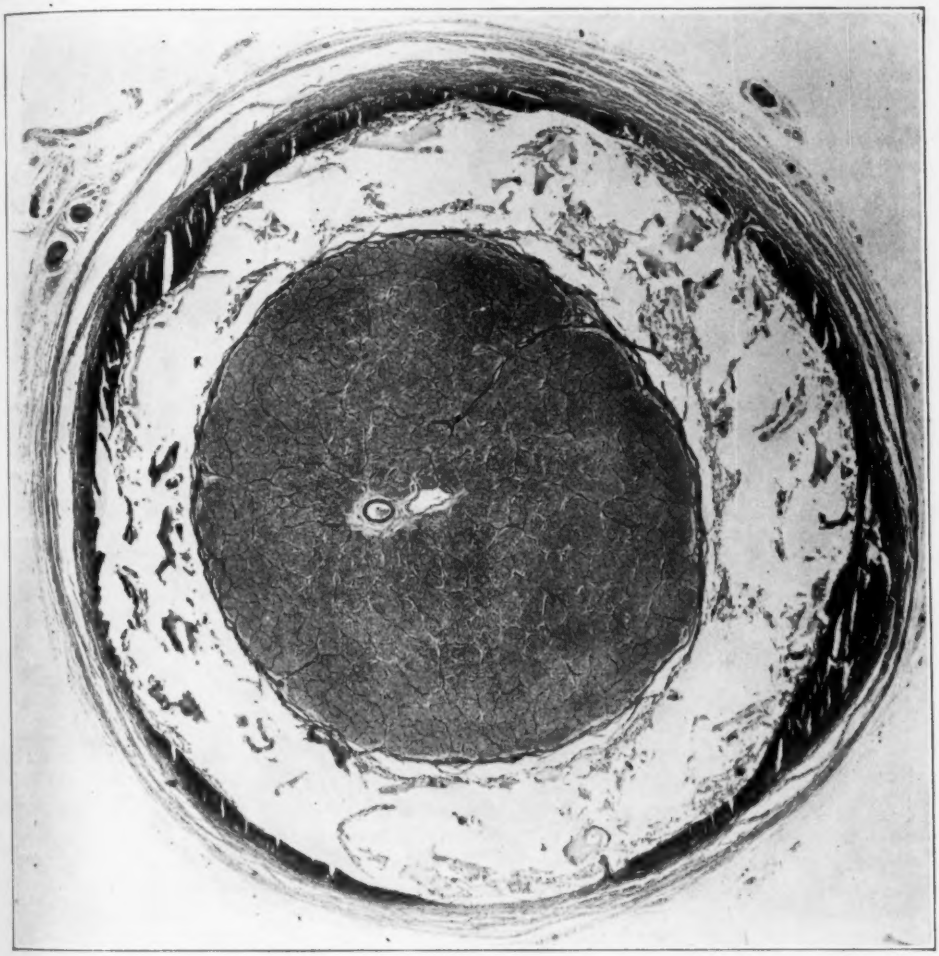

Fig. 3.—Cross section of the optic nerve, showing marked dilatation of the subarachnoid space with hemorrhage in the subdural and subarachnoid spaces. (Reproduced from United States Army Medical Museum negative 74355.)

within the pial sheath of the nerve extended from the lamina cribrosa to, but not beyond, the entrance of the central vessels. The central vein became less dilated as it passed through the lamina cribrosa and was collapsed as it passed through the subarachnoid space. Near the entrance of the central vessels, massive hemorrhage filled and dilated the subdural space. At this point the subarachnoid space was widely dilated and contained serous exudate. Hemorrhage was present but to a lesser extent than in the subdural space (fig. 3).

In a cross section of the nerve near the optic foramen there was hemorrhage in the sheath, but there was almost no dilatation of the subarachnoid space. As the entrance of the nerve

into the eye was approached, the subdural hemorrhage disappeared, but the red blood cells persisted in the subarachnoid space. No hemorrhage was seen within the nerve at any point; nor was there hemorrhage in the sclera surrounding the nerve.

Sections through the aneurysm revealed free blood in the sac, with a blood clot laid down in the wall (fig. 4). The internal elastic lamina, demonstrated by Weigert's elastic tissue stain, ended at the margin of the sac. The muscular media, stained by Van Gieson's method, was distinguishable for a short distance beyond this, but soon disappeared. For the most part, the sac wall was hyalinized and necrotic, and at one point it appeared to have ruptured.

Fig. 4.—Section through the anterior cerebral artery and the aneurysm. (Reproduced from United States Army Medical Museum negative 74353.)

SUMMARY AND CONCLUSIONS

Experimental investigations (Sicard,[22] Dupuy-Dutemps[23]) have shown that there is no connection between the subarachnoid space of the brain and the optic nerve, on the one hand, and the lymphatic spaces within the eye, on the other. Pathologic studies in cases of hemorrhage into the sheath have always proved the

22. Sicard, A.: Les injections sous-arachnoïdiennes et le liquide céphalo-rachidien, Thesis, Paris, no. 124, Paris, G. Carré & C. Naud, 1900.

23. Dupuy-Dutemps, L.: Pathogénie de la stase papillaire dans les affections intracraniennes, Thesis, Paris, no. 655, Paris, G. Steinheil, 1900.

pial sheath and optic nerve to be free from blood corpuscles. Hemorrhage has not been demonstrated in the region of the lamina cribrosa or in the sclera surrounding the entrance of the nerve. The intraocular hemorrhages are usually preretinal and frequently are situated some distance from the entrance of the optic nerve, although they may break through into the vitreous, obscuring the entire fundus.

A case is reported in which a diagnosis was made of rupture of an intracranial aneurysm associated with bilateral papilledema and subhyaloid hemorrhage in the right eye. This diagnosis was verified post mortem.

Histopathologic examination revealed marked dilatation of the central vein intraocularly, with collapse of the vein in the subarachnoid space of the nerve. There was no suggestion of hemorrhage having entered the eye from the meningeal spaces of the nerve. However, hemorrhage was demonstrated in the meningeal spaces of the nerve and anterior to the retina. These observations corroborate those of other investigators.

Some more recent reports have suggested that the intraocular hemorrhage is too great to have occurred in any other manner than by extension from the meningeal spaces of the nerve. Nevertheless, the information at hand leads one to conclude that the intraocular hemorrhage is the result of sudden and severe interference with the return venous flow of blood from the retina.

Col. J. E. Ash, curator of the United States Army Medical Museum, and his staff assisted in the preparation of the histopathologic portion of this paper.

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DISCUSSION

DR. ALGERNON B. REESE: Dr. Greear has pointed out that intraocular hemorrhage may be secondary to intracranial hemorrhage and that there has been speculation as to the relationship of the two. Some writers have thought that the intracranial hemorrhage spreads to the eye directly via the vaginal space. Dr. Greear seems to give conclusive proof, however, that the intraocular hemorrhage in his case was the result of sudden and severe interference with the return venous flow of blood from the retina by compression of the central retinal vein as it traversed the subdural space. The intracranial hemorrhage was due to rupture of an aneurysm of the circle of Willis. Similar intraocular hemorrhage may occur from intracranial hemorrhage from other causes. In a case of Dr. Grady Clay a man awoke and found the vision in the left eye poor. He had been drinking heavily for several days and the preceding night had had a vomiting attack so severe that his abdominal and thoracic muscles were sore. A fundus examination showed swelling of the left disk and many hemorrhages scattered over the fundus, not only in and adjacent to the disk but elsewhere, even far in the periphery. The vision was 20/50. In two months the papilledema and hemorrhages had almost entirely disappeared and the vision was 20/30. In four months there was no evidence of fundus changes and the vision was 20/20. I feel sure that the cause of the intraocular hemorrhage was the same in this case as in Dr. Greear's case. That is, an intracranial or intravaginal hemorrhage compressed the central retinal vein as it traversed the subdural space. The intracranial hemorrhage in Dr. Clay's case occurred because the veins of the upper part of the thorax, neck and head have no valves and therefore permit the transmission of pressure to their terminals as a result of violent compression of the abdomen and thorax. The suddenness of the compression of the central retinal vein by the intracranial hemorrhage is important in the production of intraocular hemorrhage in such cases. A gradual onset of similar compression would permit vascular compensation, and probably no such sequela as retinal hemorrhage would occur.

Dr. Greear's presentation is so cleancut and conclusive that it leaves little to be said except that his splendid contribution is much appreciated.

CONGENITAL BILATERAL ANOPHTHALMOS

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A review of the ophthalmic literature reveals that cases of anophthalmos, both unilateral and bilateral, have been reported from time to time. In many the diagnosis was based on purely physical findings. In a limited number of cases it followed serial sections of the orbital contents. If one accepts the definition of anophthalmos as the condition in which no true eyeball tissue can be found microscopically, then few cases of anophthalmos are recorded in the literature, and it becomes impossible to distinguish clinically between anophthalmos and an extreme degree of microphthalmos.

A great many embryologic abnormalities may cause suppression of an eye. According to Mann,[1] in the embryologic development of the eye three types of anophthalmos can exist. One type is caused by a failure of the optic pit to deepen and form an outgrowth from the forebrain. In a second there is a complete suppression or an abnormality of the whole of the forebrain. A third type is that in which an optic vesicle has formed, subsequently degenerated and completely disappeared.

For suppression of an optic outgrowth, the cause must be present during the period of differentiation, before the formation of the optic outgrowth but after the formation of the beginning of a forebrain. As a rule the patient has no other defect, an indication that the defect is germinal. He usually presents the following ophthalmologic picture: The eyelids are present, are kept closed and have a concave appearance, but they are otherwise normal, as are the cilia, puncta, lacrimal apparatus and meibomian glands. The conjunctival sac is small, and ankyloblepharon may or may not be present. The orbit is smaller than normal for the patient's age. The palpebral fissure is small, and the orbit may contain fat, muscles and nerves. The extrinsic ocular muscles may be present and normally innervated. The optic foramen is usually small, and no evidence of an optic nerve is present; hence there is no optic chiasm. In the case of hereditary anophthalmos in which a complete autopsy was done by Gallemaerts,[2] examination of the brain showed the external geniculate bodies and the pulvinar to be underdeveloped. The anterior corpora quadrigemina were flattened, and the posterior corpora quadrigemina were not as large as normal. The history strongly suggested a genetic tendency to suppression of the optic outgrowths, in that the mother had extreme unilateral microphthalmos, though the father was normal. The inheritance from an affected female agrees with Yudkin's[3] experimental work on a strain of white rats, which showed that hereditary anophthalmos can be transmitted through affected females when they are mated with unrelated males. The affected males did not transmit this defect when mated with normal females.

1. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937.

2. Gallemaerts: Anophthalmie congenitale et familiale, Ann. d'ocul. **161**:490, 1924.

3. Yudkin, A. M.: Congenital Anophthalmos in a Family of Albino Rats, Am. J. Ophth. **10**:341, 1927.

Stockard [4] has shown that when the eggs of fish are subjected during early stages of development to the action of weak solutions of alcohol, the resulting embryos show marked abnormalities in the structure of the central nervous system and organs of special sense. Such specimens either have small eyes with poorly differentiated retinas, are cyclopean, are asymmetrically monophthalmic or are anophthalmic. The ophthalmic defects sometimes occur in as many as 98 per cent of the specimens. Lewis,[5] Spemann [6] and later workers have shown that by the application of various methods, usually chemical, at a certain definite stage, anophthalmic embryos can be produced. The chemical agent must take effect at a time when the optic outgrowths are just beginning.

Monstrosities with associated anophthalmos that usually do not live are the end result of the complete suppression of the forebrain. It has been shown that they can be produced experimentally in Amphibia by altering the salt concentration of the surrounding medium at a certain period in the differentiation of the embryo. The hypothesis is therefore put forth that such abnormalities occur as a result of some unfavorable environmental change early in the pregnancy and hence are not of germinal origin.

There have been reports of embryos with different-sized optic cups, one being normal and the other small and not in contact with the surface ectoderm. When this anomaly occurs the smaller optic cup may give rise to extreme microphthalmos or may disappear completely. It probably is the causative factor in cases reported in the literature in which there is a fibrous mass with pigment tissue present, nerve elements absent and extrinsic muscles present.

The number of recorded cases of anophthalmos is extremely small, since most of the similar cases reported were not subjected to microscopic study and are not instances of anophthalmos as previously defined. A study of the literature shows no marked predilection for one sex, and, while some cases show heredity as a factor, there are not many in the literature to support this view. Usually there is no history of consanguinity or of congenital abnormalities in the parents or other members of the family. Since anophthalmos occurs bilaterally as a rule, it is probably caused by some environmental factor acting at the optimum time and having a specification on the highly specialized ocular tissues. The cases in which there are apparently familial and hereditary factors can be explained on a germinal basis.

The following 2 cases illustrate the variations that may occur in so-called cases of anophthalmos. The variations are not only in the size of the orbits and the adnexa of the eyes but in the mental development of the 2 patients, in which there was considerable difference.

REPORT OF CASES

CASE 1.—*History.*—R. W., a white boy born Nov. 29, 1939 of normal parents, had two older sisters, who were normal mentally and physically. He was a nine month, spontaneously delivered infant. There was no history of consanguinity of the parents or of ocular defects in any member of the parents' families. His birth weight was 8 pounds and 12 ounces (3,969 Gm.), and, aside from the ocular defect, the physical condition was normal. At the age of 6 months the height was 25 inches (63.5 cm.) and the weight 14 pounds and 7 ounces (6,549 Gm.). At the

4. Stockard, C. R.: The Influence of Alcohol and Other Anaesthetics on Embryonic Development, Am. J. Anat. **10**:369, 1910.

5. Lewis, W. H.: Experimental Studies on the Development of the Eye in Amphibia, Am. J. Anat. **6**:473, 1906-1907.

6. Spemann, H.: Ueber correlationeninder Entwickelung des Auges, Ant. Anz. (supp.) **19**:61, 1901.

age of 1 year the height was 30 inches (76 cm.) and the weight 25 pounds (11.3 Kg.). The developmental history shows that he had his first teeth at 4 months, began to creep at 8 months and was able to sit up after certain unique physical maneuvers at the age of 10 months. At the age of 1 year he reached sitting and standing positions with a minimum of difficulty. He did not start to walk until the age of 2 years or to talk until 22 months. His mental development was normal from earliest childhood, and he had always been social in behavior. At the age of 13 months he was rated as having an intelligence quotient of 80 according to the Kuhlman test.[6a] This was not thought to be a fair estimate of his ability.

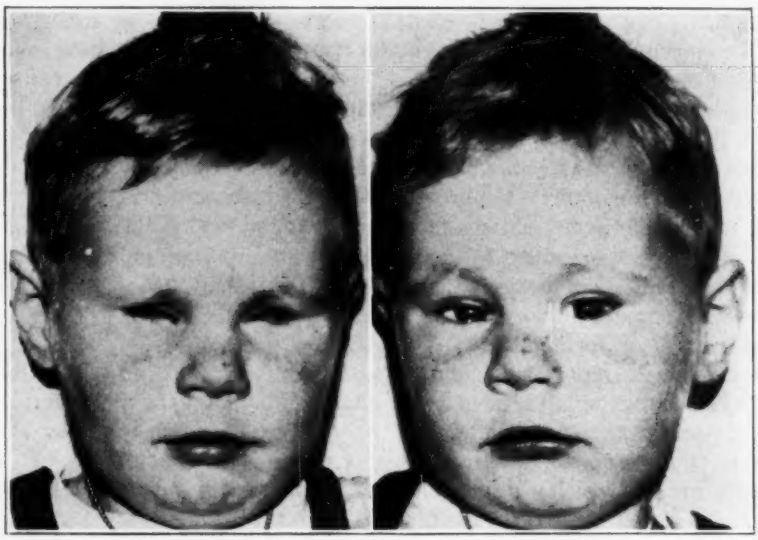

Fig. 1 (case 1).—The patient without prostheses and with prostheses. The change in his appearance is obvious.

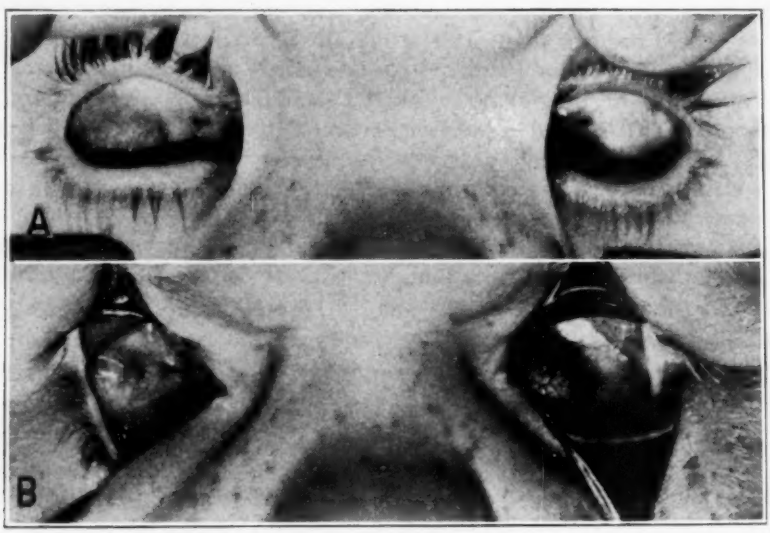

Fig. 2 (case 1).—Photographs of the sockets, showing pseudoepicanthus due to spreading of the lids (*A*). The cystic mass is visible in the lower nasal quadrant of the left orbit (*B*).

6a. Dr. S. Stinchfield-Hawk, University Southern California, performed the intelligence quotient tests.

It is of interest to note that until the age of 13 months the patient was cared for at home by his parents under the supervision of a competent pediatrician. He received excellent physical care, and, although the parents attempted to aid him, they were unable to develop his inherent potentialities. At about the age of 15 months he was placed in a nursery school for visually handicapped children. He was retested eighteen months later with the Hayes-Irwin adaptation test for the blind, scoring 123, and he scored over 112 in the Kuhlman test. At the time of writing he scores 100 per cent in speech, memorizes easily and is precocious in sound discrimination, being able to sing and carry a tune. He is therefore within the upper limits of normal with regard to intelligence quotient.

Physical Examination.—The patient was well developed and well nourished at the age of 2 years and 7 months and was active. He had excellent muscular development and tone, with skin of normal texture and no blemishes. The head was well shaped and symmetric, with no exostoses. The hearing was normal, the ear drums intact and the nose and throat normal. The thyroid was not enlarged, no cervical adenopathy was present, the heart was normal in size and no murmurs were heard, the lungs were normal to percussion and the breath sounds were normal. The liver and spleen were not palpable, and no masses were present in the abdomen. The genitalia were normal. The extremities were all normal, with no limitation of motion. The normal reflexes were present, active and equal. The patient's movements were well coordinated and his walking posture good.

The height was 35 inches (89 cm.) and the weight 30 pounds (13.6 Kg.). Wassermann and Kahn tests gave negative results. A roentgenogram of the skull showed a normal calvarium and sella turcica, absence of the frontal sinuses and normal development of the antrums.

Table 1 shows the percentage by which the orbits were smaller than those of a normal child the same age.

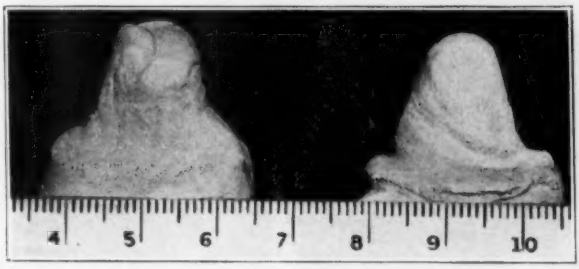

Fig. 3 (case 1).—Molds of the orbits. The depth is the distance from the apex of the mold to the base of the ridge and not to the surface in contact with the rule.

TABLE 1.—*Comparison of the Orbits of Patient 1 with Those of a Normal Child the Same Age*

	Percentage Smaller
Transverse meridian	25
Longitudinal meridian	32
Right oblique meridian	26
Left oblique meridian	41

Ophthalmologic Examination.—Right Orbit: The skin of the lids, free margins of the lids, cilia, puncta and lacrimal apparatus were normal. The lids were closed, but the free margins did not approximate each other, there being an interpalpebral fissure measuring approximately 2 mm. (fig. 1). There was a moderate flow of tears when the patient cried. The inner surfaces of the lids were covered with normal-appearing conjunctiva, and the tarsal plates were normal. The length of the palpebral fissure was 20 mm. Palpation of the orbit revealed in the lower temporal quadrant a small cystic mass, beneath which the optic nerve could be palpated. The movement of the mass simulated the movement of an eye by the extraocular muscles, but there was much less motility.

The entire surface of the mass was covered with conjunctiva, and in the center was a circular area about 5 mm. in diameter which resembled degenerated corneal tissue. About 3 mm. nasally and upward from this area there was a circular, bluish spot about 1 mm. in diameter, which resembled iris tissue.

Left Orbit: The appearance was the same as that of the right eye except that the cystic mass was situated in the lower nasal quadrant of the orbit (fig. 2*B*). The interpalpebral

Fig. 4 (case 1).—The sella turcica.

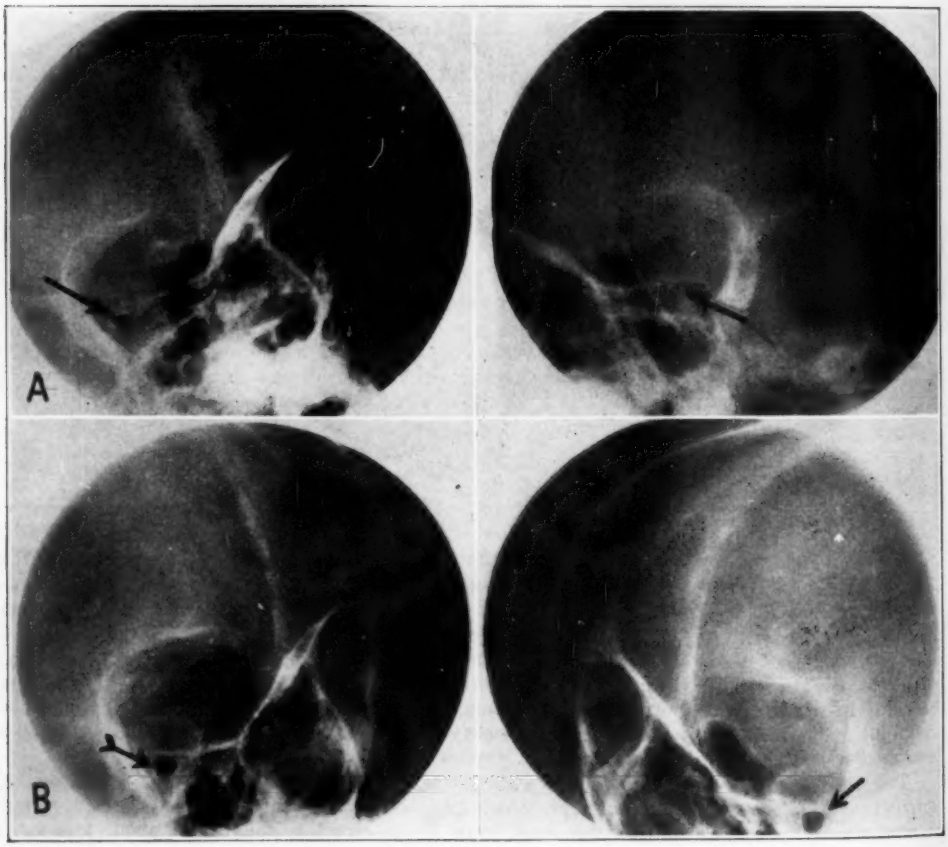

Fig. 5 (case 1).—The optic foramens of patient 1 (*A*), which are somewhat oval and small in comparison with those of a normal child the same age (*B*).

fissure with the lids closed measured approximately 3 mm., and it was 20 mm. long. The lids could be opened to give the fissure a maximum width of 12 mm. The depth of the orbit was 20 mm.

CASE 2.—*History.*—R. B., a white boy born March 17, 1935, the only child of parents who were normal mentally and physically, had been spontaneously delivered at nine months. There was no history of consanguinity of the parents, no physical defect in either parent and no history of congenital defects in members of the parents' families. The only physical abnor-

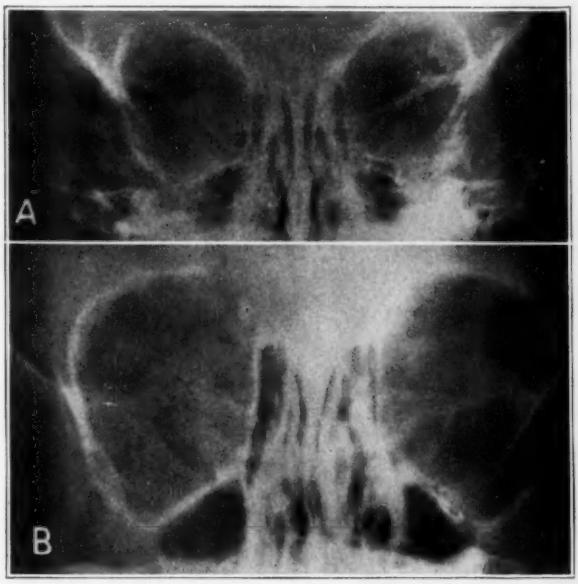

Fig. 6 (case 1).—Anteroposterior roentgenograms illustrating the pronounced smallness of the orbits of patient 1 (*A*) as compared with those of a normal child the same age (*B*).

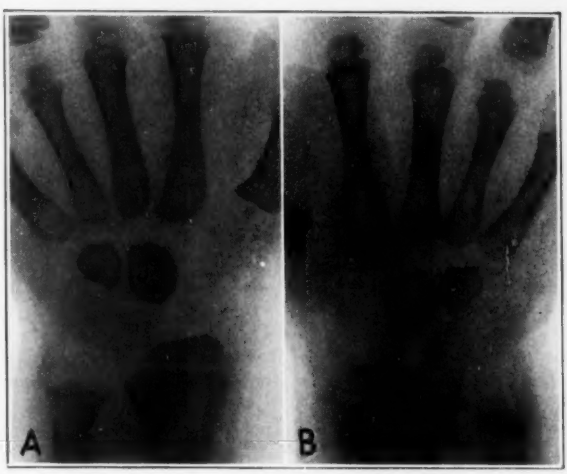

Fig. 7 (case 1).—Roentgenograms taken of the wrists to determine the developmental status of the osseous system. They show a bone age of 2 years. According to the standards of both E. K. Shelton (Roentgenographic Studies in Normal Osseous Development, *J. A. M. A.* **96**:759 [March 7] 1931) and T. W. Todd (Atlas of Skeletal Maturation, St. Louis, C. V. Mosby Company, 1937), the development was a year retarded, but both observers have said that such a variation may be within normal limits. (*A*, left; *B*, right.)

mality of the patient at birth was the bilateral anophthalmos. The birth weight was 8 pounds and 14 ounces (4,026 Gm.) and the height 21 inches (53 cm.). The development from birth to the time of writing has been unsatisfactory both mentally and physically, perhaps owing partly to the parents' inability to help him and partly to the congenital defect. The patient did not talk or walk before the age of 3½ years, at which time he was placed in a school for visually handicapped children. Under the supervision of a trained nurse he started to walk about one month after admission, but his progress since then has been slow. On admission the musculature was poorly developed and the muscle tone and coordination extremely poor. After being in the school for about a year he started to talk. His progress was retarded because he was a day student from October 1938 to June 1939 and made no progress at home, since his parents were completely unable to aid him. He lived at the school from June 1939 to January 1940, during which time he made considerable progress in walking and talking. He showed evidence of a fairly good memory, and remembered the names of other children by their voices. He was social in his behavior and was taught to express his needs fairly well.

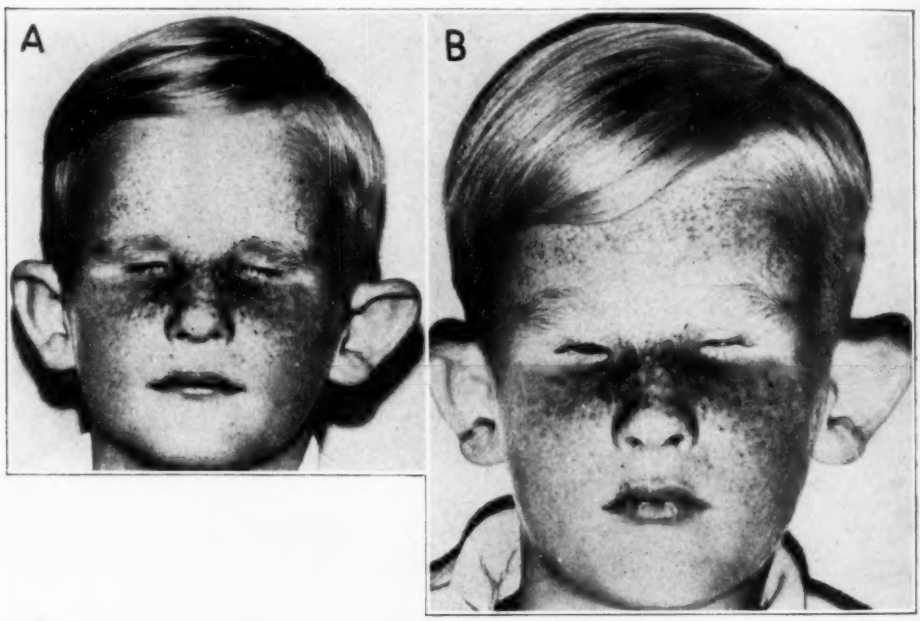

Fig. 8 (case 2).—*A*, the patient, without protheses. Before this patient will be able to wear prostheses it will be necessary to perform canthoplasties and one of the classic operative procedures to increase the depth of the cul-de-sacs. *B*, the patient voluntarily opening his lids, showing the smallness of the lids and the difference in size of the palpebral fissures, the left being much smaller than the right.

During the next year and a half he was again under his parents' care, and he retrogressed to the point where he stuttered and had difficulty in beginning sentences and expressing his wishes. At the time of writing he is listless, lacks curiosity and does not remember three simple commands. His posture is again poor, though it was good for an interval under the direction of the school nurse.

In the Hayes-Irwin test which, because of speech blocking, fatigue and lack of ability to cooperate actively, was the only test in which a satisfactory response could be obtained, he rated an intelligence quotient of 62 (chronologic age, 7 years and 3 months), a 4 per cent drop from the result (66) of a test performed about one year earlier.

Physical Examination.—The patient was a thin, poorly developed white boy aged 7, who lay listlessly in bed. His skin was of normal texture, with no blemishes. His muscular development, tone and coordination were poor. The head was somewhat dome shaped and asymmetric, with no exostoses. The ears protruded from the head, the drums were intact and the hearing was normal. The nose and throat revealed no abnormality. The thyroid

gland was not palpable, and cervical adenopathy was not present. The chest wall was poorly developed, the heart was not enlarged and no murmurs were heard. The lungs were normal to percussion and the breath sounds were normal. The liver and spleen were not palpable, there were no masses in the abdomen and the genitalia were normal. The extremities were normal, with no limitation of motion. The normal reflexes were all present, active and equal.

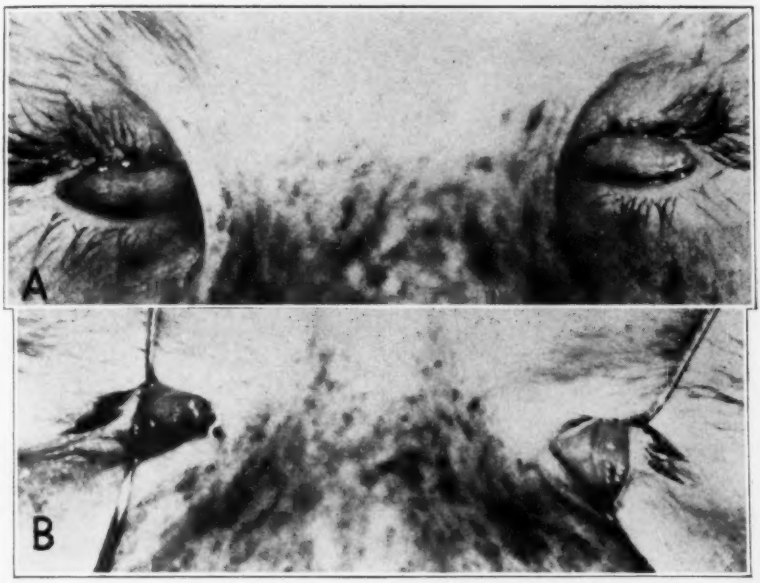

Fig. 9 (case 2).—*A*, close-up photograph illustrating the shallow sockets. The pseudo-epicanthus is due to the spreading of the lids. *B*, the small lids and the narrow palpebral fissures.

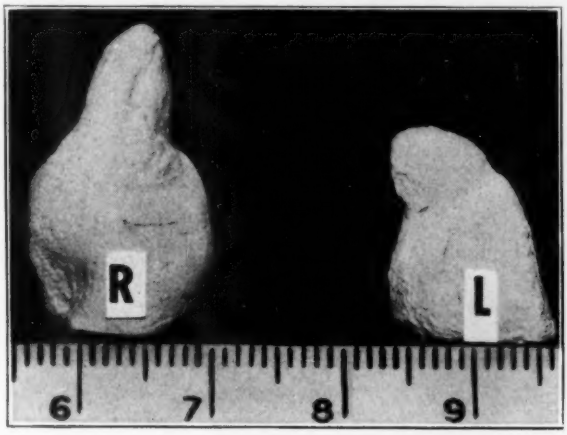

Fig. 10 (case 2).—Molds of the orbits. The depth is the distance from the apex of the mold to the base at the ridge and not to the surface in contact with the rule.

TABLE 2.—*Comparison of the Orbits of Patient 2 with Those of a Normal Child the Same Age*

	Percentage Smaller
Transverse meridian	37
Longitudinal meridian	33
Right oblique meridian	35
Left oblique meridian	36

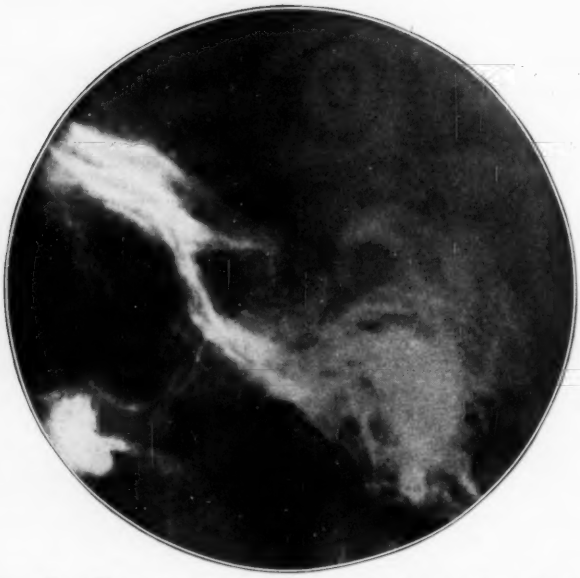

Fig. 11 (case 2).—The sella turcica, showing fusion of the clinoid processes.

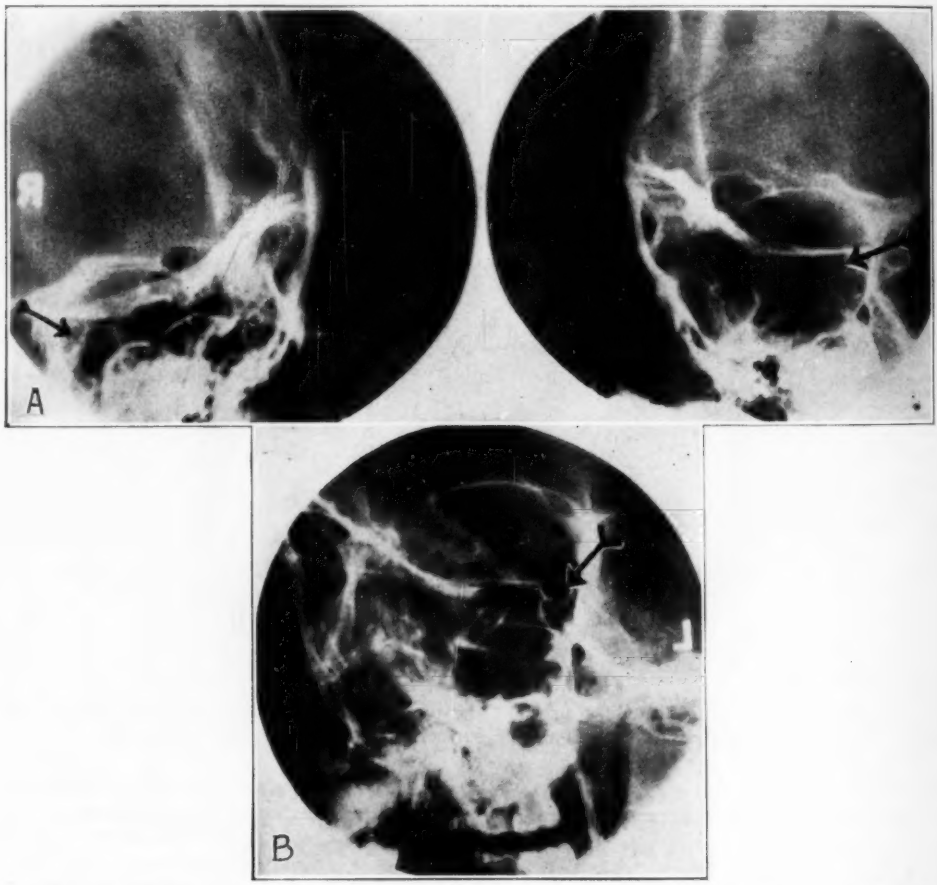

Fig. 12 (case 2).—*A*, a roentgenogram illustrating the absence of optic foramens. *B*, optic foramen in a normal child of the same age.

Wassermann and Kahn tests gave negative results. The weight was 42 pounds (19 Kg.) and the height 47 inches (119 cm.). Roentgenograms of the skull showed a peculiar cranial formation with a microsella. The anterior and posterior clinoid processes from three different angles appeared to be fused. According to Shelton [7] this probably had no clinical significance, although possible embarrassment of pituitary function during the intrauterine period should be considered.

Table 2 shows the percentage by which the orbits were smaller than those of a normal child the same age.

Ophthalmologic Examination.—Right Orbit: The skin of the lids, the cilia, the puncta and the lacrimal apparatus were normal. The lids appeared concave and were closed, and the free margins approximated each other. The conjunctiva of the lids and tarsal plates was normal. There was a moderate flow of tears when the patient cried. The lids were small, and the

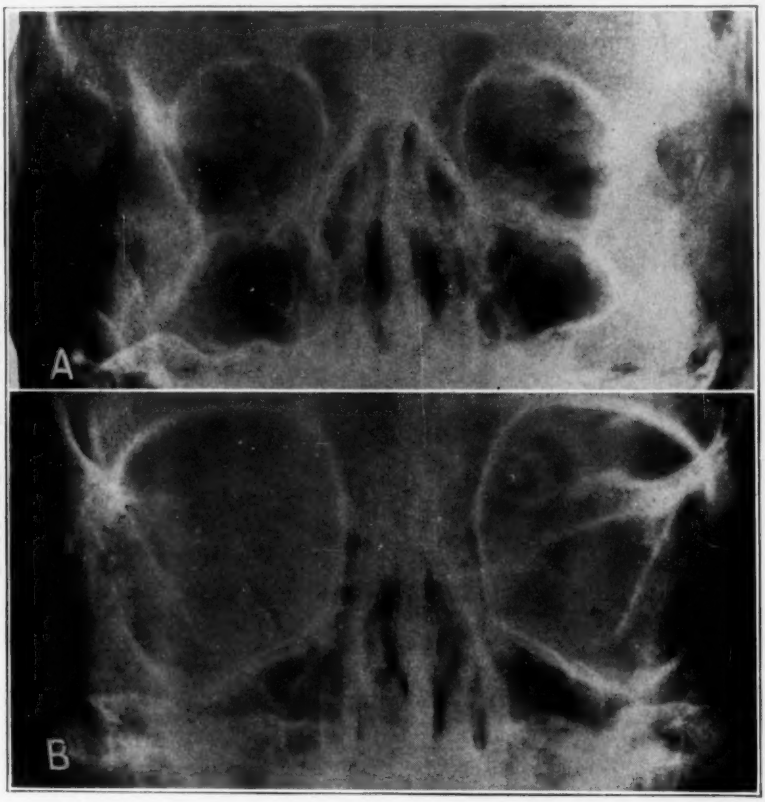

Fig. 13 (case 2).—*A,* an anteroposterior roentgenogram illustrating the smallness of the orbits. *B,* the orbits of a child the same age who is physically and mentally normal.

palpebral fissure was 13 mm. long. The lids could be opened only far enough to make this fissure 10 mm. wide. On palpation, no mass or optic nerve could be felt in the orbit. The conjunctiva covering the socket was normal. The depth of the orbit was 14 mm.

Left Orbit: The appearance was the same as that of the right orbit except that the lids were smaller, this side of the face being less developed than the right. The palpebral fissure was 11 mm. long. The lids could be opened only far enough to make the fissure 8 mm. wide. The orbit measured only 8 mm. in depth.

COMMENT

Two cases of congenital bilateral anophthalmos are presented, together with photographs to show the improvement in the appearance in one case after the

7. Shelton, E. K.: Personal communication to the author.

fitting of prostheses, the value of which cannot be doubted. The psychologic effect of artificial eyes on a young child is indirect. The reaction of other persons toward him, as they accept or reject him, influences his emotional and physical progress or retardation.

A physical handicap in a child is an emotional trauma to his parents. To have the child unsightly, in addition, heightens the parents' resentment, which may seem to be completely repressed but nevertheless has an effect on their conduct toward the child. Instead of simply accepting him as a disabled and handicapped person, they tend either to reject him openly or, more frequently, to overprotect him. In both situations he is hampered from fully developing his potentialities. A child whose appearance is improved by artificial eyes (patient case 1) is certainly more acceptable to his parents, relatives and future associates

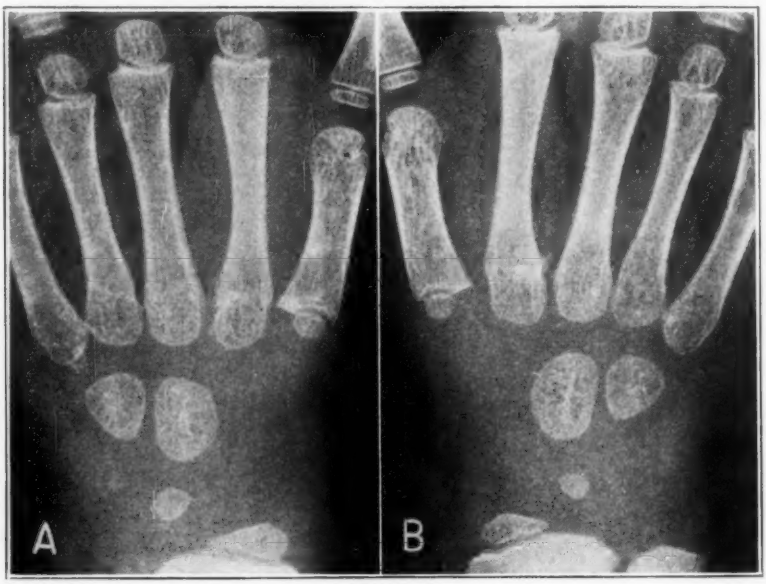

Fig. 14 (case 2).—Roentgenograms taken of the wrists to determine the developmental status of the osseous system. They show a bone age of only 3 years. Therefore, according to the standards of both Shelton and Todd, the patient was nearly five years retarded. According to Shelton, true mongolism, other forms of mental deficiency and birth injuries do not consistently retard the development of the osseous system, although hypothyroidism is occasionally associated with retardation and must consequently give a confused picture (*A*, left; *B*, right).

than one who is disfigured (patient 2). As a person who is as nearly physically normal as possible, he is better equipped emotionally to face life.

Most parents are at a complete loss as to how to aid a child handicapped by such a deformity. The need of placing a child with bilateral anophthalmos under the care of a trained worker cannot be too strongly stressed. Unless this is accomplished early, the child may be handicapped both mentally and physically.

When the eyelids are small and the socket too shallow to accommodate a prosthesis, a canthoplasty and some operative procedure to increase the depth of the superior and the inferior cul-de-sac must be performed.

409 North Camden Drive.

BILATERAL UVEITIS, POLIOSIS AND RETINAL DETACHMENT WITH RECOVERY

REPORT OF A CASE

ISADORE GIVNER, M.D.
NEW YORK

Harada,[1] in 1926, first described bilateral detachment of the retina in the course of low grade uveitis as an independent disease. The typical onset of an acute diffuse exudative choroiditis or uveitis accompanied by poliosis, and sometimes alopecia and deafness, with a relatively favorable prognosis for spontaneous retinal reattachment, warrants consideration of this disease as an entity. It is invariably bilateral. The onset is acute, is accompanied by headache and occasional vomiting or nausea and is characterized by low grade inflammatory symptoms in the anterior segment of the uvea. In the early stage opacities of the vitreous and edema of the disk suggestive of papillitis are present; these are followed by an extensive detachment. The detachment has a definite tendency to disappear within a few weeks, and the healing results in good visual acuity. The fundi show much depigmentation, and in the periphery white patches suggestive of sympathetic choroiditis are found.

In trying to determine the cause of this condition, Takahashi [2] inoculated rabbits with vitreous from affected eyes. The fluid did not contain micro-organisms. With intracisternal inoculations, in 2 of 5 instances he produced a descending optic neuritis and uveitis. Inoculation of cerebrospinal fluid from the patient into the vitreous produced inflammation in 1 of 4 rabbits. Inoculation of the cisterna with brain tissue from an infected animal produced optic neuritis and iridocyclitis. Direct inoculation into one eye produced inflammation of that eye and of the other eye by way of the optic nerve.

Tagami's [3] inoculation of the vitreous of rabbits with subretinal fluid also resulted in uveitis, which histologically resembled sympathetic uveitis except for the absence of giant cells. The infiltration of the choroid consisted of large mononuclear elements. Furthermore, detachment of the choroid and retina through serofibrinous exudate and degeneration of the pigment epithelium, with almost negligible changes within the retina, took place. This suggested classification with the virus diseases.

Okamura,[4] on the other hand, reported 2 cases, in 1 of which there was secondary glaucoma necessitating iridectomy. Histologic examination showed giant cells of the Langhan type. In the second case the uveitis was of tuberculous origin.

In this country, Andrew Rados [5] is the only author who has reported a case of Harada's disease. He reported 2 and concluded: "The discrepancy in the mechanism between virus disease and tubercular origin is widespread and cannot be answered at present dogmatically." The association of poliosis with an inflammatory change in the eyes, namely, sympathetic ophthalmia, was first noted, in

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Read before the New York Academy of Medicine, Section of Ophthalmology, Jan. 18, 1943.

1. Harada, cited by Salus.[10]
2. Takahashi, M.: Acta Soc. ophth. jap. **35**:114, 1931.
3. Tagami, K.: Acta Soc. ophth. jap. **35**:114, 1931.
4. Okamura: Acta Soc. ophth. jap. **41**:679, 1937; **42**:196, 1938.
5. Rados, A.: Bilateral Uveitis Associated with Detachment of Retina (Harada's Disease), Arch. Ophth. **23**:534 (March) 1940.

1873, by Schenkel. Hutchinson,[6] twenty years later, was the first to describe poliosis associated with bilateral iridocyclitis. When there is a change in the air content the whitening of the lashes may be sudden, and this fact explains the occurrence of canities overnight. In such instances there is a complete absence of pigment in the hair shaft. When a disturbance of pigment is the cause of the graying, the process occurs less rapidly, the color is less distinctly white and a few granules may be seen between the cells of the hair shaft.

The following case is presented, first, because of the rarity of the disease; second, because an attempt was made to determine the causation, and, third, because of the opportunity presented for evaluation of the methods employed in handling this condition.

REPORT OF CASE

T. M., a youth, aged 20, of Italian extraction, was first seen June 13, 1939. He stated that on May 22 he noticed that the vision of his right eye was failing and two days later his left eye became affected. He had been employed as a painter off and on for fourteen months. His duties entailed mixing of paints, but occasionally he was exposed to the fumes from the burning off of the paint. He went to see his family physician, Dr. P. J. de Bell, who found stippling of the red cells. The patient had cramps in his stomach and legs when he walked excessively. Dr. de Bell considered this a case of lead poisoning and administered calcium and vitamin B. No determinations for lead were done, however.

When the patient was referred to me, his vision was 5/200 in his right eye and counting of fingers at 4 feet (122 cm.) in his left eye. There were many deposits on the posterior surface of each cornea. Ciliary injection was present, but no ciliary tenderness. The pupils measured 5 mm. and were fixed to light, both direct and consensual, and in accommodation, owing to plastic iritis. The tension was normal. The vitreous of each eye contained fine opacities.

The disks were congested, with the margins ill defined. In the macular regions, however, was noted the most outstanding finding, that is, a detachment of the macula in each eye, the foveal region being 6 D. higher than the level of the disks (fig. 1).

By June 27, the vision of both eyes had improved to 20/70 and the macular detachment had disappeared, leaving areas of depigmentation and condensation in both macular regions, with no foveal reflex. The optic nerves, however, were still congested (fig. 2).

By July 6, the nerve heads showed less congestion, and with a compound myopic astigmatic correction of -0.50 D. sph. $\bigcirc$ -0.50 D. cyl., axis 180, 20/50 vision was obtained in each eye. The visual field tested with a 3/330 object showed a nasal and inferonasal contraction to 40 degrees in the right eye and a temporal contraction to 70 degrees in the left eye. Both blindspots were enlarged.

On August 1 the vision was $20/25 + 2$ in the right eye and 20/30 in the left.

Up to this time the patient had not been faithful in keeping appointments, so that lead studies could not be done. However, on October 25, both blood and urine were checked for lead and were found to be normal: 0.004 mg. per hundred cubic centimeters of blood (normal, 0.00 to 0.05 mg.) and 0.07 mg. in a twenty-four hour output, or 900 cc. of urine (normal, 0.00 to 0.05 mg.).

The Wassermann reaction was negative. The Mantoux reaction was negative with a 1:20,000 dilution but 2 plus with a 1:7,500 dilution. Roentgenograms of the chest, teeth and sinuses were normal. The patient had been receiving systemic potassium iodide and vitamin therapy and local atropine and cocaine therapy. His fields were now normal for a 3/330 white object, and by August 31 the vision was 20/20 in the right eye and $20/30 + 3$ in the left with a correction of -0.50 D. cyl., axis 180.

The patient disappeared from observation for seven months, and when seen March 30, 1940 he stated that three weeks previously his lashes had turned white, be believed overnight.

Examination disclosed poliosis of both eyes (fig. 3). There had been a marked increase in the deposits on Descemet's membrane; corneal edema was present and the tension was 65 mm. in the right eye; at the nasal edge of the right pupil, Koeppe's nodules were seen and there were similar deposits on the capsule of the lens. In the fundus of each eye were seen diffuse small chorioretinitic areas; these were more clearly observed in the left eye. The Koeppe nodules being interpreted as allergic, the patient was given histaminase (torantil). Extremely weak doses of tuberculin, a dilution of 1:40,000,000 to start with, and epinephrine bitartrate, a 2 per cent solution instilled locally, were used. This treatment did not reduce

6. Hutchinson, J.: Arch. Surg., London **4**:357, 1892-1893.

the tension or quiet the process. A paracentesis was performed and the aqueous cultured on Petroff's medium for tubercle bacilli, with negative results. The paracentesis was repeated daily for four days, but the tension was not controlled. The fields were still good.

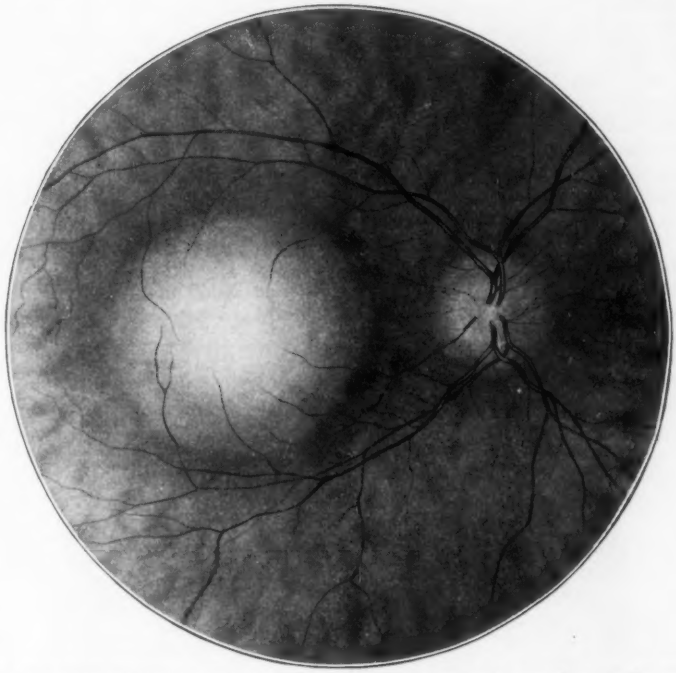

Fig. 1.—A drawing depicting the detachment in the macular region as it appeared in the beginning of the disease.

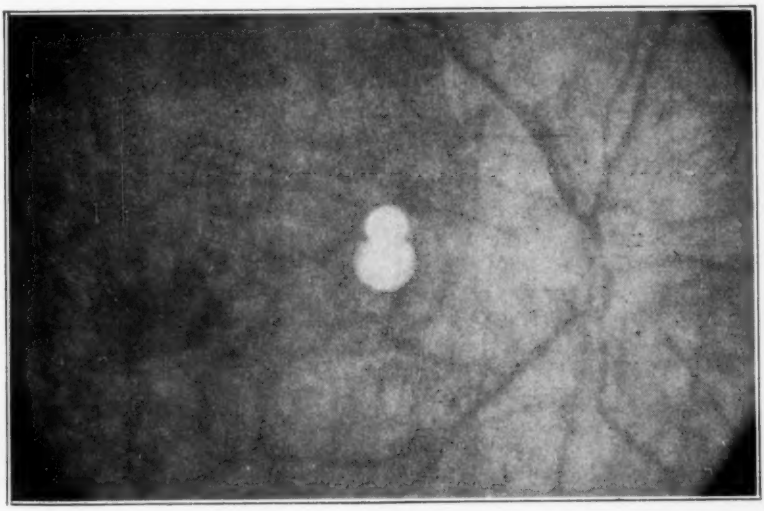

Fig. 2.—A print from a kodachrome film showing the areas of depigmentation and condensation in the macula after the detachment had disappeared.

The patient was admitted to the New York Eye and Ear Infirmary, and with a course of sulfanilamide, rest and plenty of vitamins, including vitamin P, the tension returned to normal. The general examination gave negative results throughout. The patient was allergic to

atropine; so scopolamine hydrobromide, 0.5 per cent, was substituted. A tuberculous origin still being considered, he was again given injections of weak tuberculin and he now showed a general reaction, as evidenced by elevation of the temperature, to a dilution of 1 : 500,000,000, so that this strength could not be increased.

In May 1940 his tension was normal in both eyes but both corneas were studded with precipitates. His vision, however, was 20/20 in the right eye with a correction of —5.50 D. sph. ⌒ —0.75 D. cyl., axis 180, and 20/25 in the left with a correction of —1.50 D. sph. ⌒ —0.50 D. cyl., axis 180. The original refraction was —0.50 D. sph. ⌒ —0.50 D. cyl., axis 180, for both eyes. This increase in the myopia could not be explained by swelling of the lens, and it had been present previous to the sulfanilamide therapy. Uveitis has been considered an explanation for such myopia.

Short wave therapy was used for two applications but seemed to aggravate rather than aid the condition. The patient was next given AO tuberculin obtained from Japan; this is supposed to have removed the lipoid capsule that is claimed to cause the untoward allergic response. By its use I hoped to improve the antigenic response. No improvement was noted; however, no reaction occurred.

In July 1940 the vision was 20/70 in the right and 20/30 in the left eye. The field was contracting owing to the secondary glaucoma, which now, in spite of daily paracenteses for over two weeks, stayed high.

Studies for undulant fever gave negative results. Reactions to aqueous injected into guinea pigs were negative for tuberculosis.

Gold sodium thiosulfate, 5 mg. in 5 cc. of sterile distilled water, was given without beneficial effect. There was practically no nasal field for the right eye. The tension had gone up in the left eye to 50, but the field was still normal. Vision in the right eye was 10/200 and in the left 20/30 with correction.

Fig. 3.—The patient's eyes, showing poliosis.

Dr. Arnold Knapp saw the patient with me in consultation and advised studies at the Medical Center. Through the assistance of Dr. Phillips Thygeson and Dr. Ludwig von Sallmann tests were carried out and gave the following results:

1. A series of chorioallantoic and yolk sac inoculations produced no virus growth, aqueous and iris tissue removed by Dr. John H. Dunnington being used. Dr. Dunnington performed bilateral iridectomies and sclerectomies for control of the glaucoma.

2. Intraperitoneal guinea pig inoculations of ground iris tissue gave negative reactions for tuberculosis.

3. Inoculations of ground iris tissue into the anterior chamber of a guinea pig gave only a temporary reaction due to the accompanying trauma of the inoculation.

4. The cornea of a rabbit tested by the scratch method, as well as the anterior chamber of another rabbit, inoculated with iris tissue, revealed nothing significant.

5. A smear of ground iris tissue failed to show elementary bodies, and culture did not reveal bacteria. Pieces of iris tissue were fixed and stained with hematoxylin and eosin. Infiltration of round and plasma cells was present and was interpreted as evidence of the chronicity of the process. Here and there were seen eosinophils (fig. 4). Iris tissue stained by the Ziehl-Neelsen method did not show tubercle bacilli.

Eosinophils frequently are recognized as a feature of allergy. According to Hajos and Mazgon[7] they are concerned in desensitization. Olson's[8] recent studies of the eosinophils

7. Hajos, H., and Mazgon, R.: Ztschr. f. d. ges. exper. Med. **68**:767, 1929.

8. Olson, in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, vol. 1, p. 219.

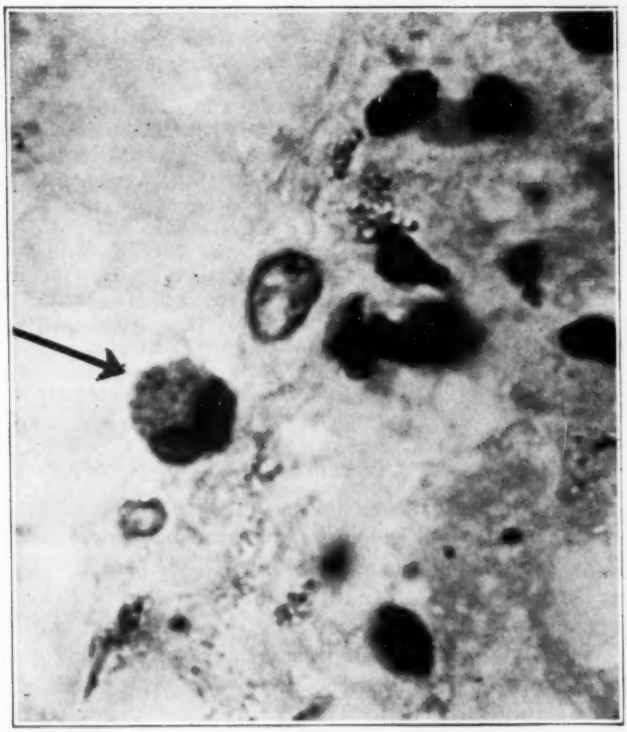

Fig. 4.—A photomicrograph of iris after removal, showing a bilobed eosinophil.

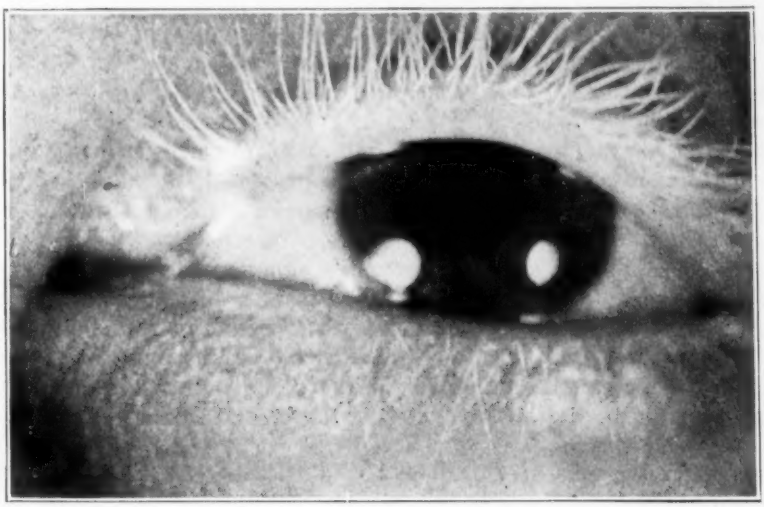

Fig. 5.—The anterior portion of the globe in its final stage. The site of the iridectomy above is partially seen.

in immune reactions indicate that a specific sensitizing product is formed in reaction between eosinophilic leukocyte granules and complex proteins.

An intracutaneous pigment test was done. The skin removed after two weeks was fixed in solution of formaldehyde and stained with hematoxylin and eosin. In the subcutaneous tissue was a fairly large amount of pigment granules, most of which lay free. At one site there were phagocytic cells of the epithelioid type, some of which contained pigment and granules. Except for this one site the picture was not like that characteristic of sympathetic ophthalmia. The interpretation was doubtful. The general examination, including a test of the hearing and an examination of the stool for ova, revealed nothing significant. The bilateral iridectomies and sclerectomies performed by Dr. Dunnington, November 27, were successful in controlling the tension and quieting the process (fig. 5).

On Jan. 9, 1941 a patch of white hair on the patient's head was first noted. The tension was normal. The vision was 10/200 in the right eye and 20/40 + in the left. The opacities in each eye were much fewer and the deposits on Descemet's membrane reduced in number. The fundi showed diffuse healed chorioretinitic areas as well as changes in the macula, as noted before. The patient was last seen Jan. 10, 1943. The vision was 20/200 in the right eye with a correction of —3.00 D. sph. and 10/200 in the left eye, or 20/20 with a correction of —2.75 D. sph. ⌒ 0.75 D. cyl., axis 15. The fields were normal in the left eye; the superior nasal field was lost in the right. The fundi were seen clearly. The tension was 18 in each eye. Very fine opacities of the vitreous, as well as old deposits in Descemet's membrane, remained in each eye.

CONCLUSIONS

1. The negative results of culture have no finality in their interpretation. The detachment, Koeppe nodules and iridocyclitis may be an allergic reaction to bacterial proteins. That the patient had an allergic factor is evident by his inability to use atropine and his untoward reaction to tuberculin in extremely weak doses at certain intervals in his history. Lead poisoning as the precipitator of the attack has to be considered, even though no one would say that lead explains the whole picture. However, questions relating to an association with heavy metals should at least be put when one is taking the history, as it is known that alopecia is sometimes associated etiologically with metallic poisoning.

2. As to the use of AO tuberculin, Nakamura [9] has reported good results in treatment of exudative uveitis and sympathetic ophthalmia by this means.

3. The fact that the patient had anterior uveal involvement does not exclude Harada's disease, as Salus,[10] the first European to publish an observation on this disease, had a patient with involvement of the anterior segment marked by deposits on the posterior surface of each cornea and nodules in the iris. Also, the absence of a complete retinal detachment, such as that originally described by Harada, would seem to me not to be a vital factor in disproving the diagnosis, as it is possible that flat detachments may have been present at the time of the macular detachment and not recognized because of the haze over the vitreous. Confirmatory evidence of this finding are the diffuse scars of previous chorioretinitis scattered inferiorly in the right eye and over the entire fundus in the left eye. The probability that this case was one of the Vogt-Koyanagi syndrome cannot, however, be ruled out. Carrasquillo,[11] who thoroughly reviewed the literature on this subject up to September 1942, found that alopecia occurred in only 53 per cent of the cases and not invariably, as stated by Duke-Elder. Poliosis was the most frequent accompaniment, occurring in 82 per cent of the reported cases. Vitiligo occurred in 62 per cent and dysacousia in only 50 per cent. The author concluded that nontraumatic bilateral uveitis accompanied by one or all of these symptoms should be regarded as the Vogt-Koyanagi syndrome.

9. Nakamura, B.: Klin. Monatsbl. f. Augenh. **89**:43, 1932.

10. Salus, R.: Klin. Monatsbl. f. Augenh. **89**:84, 1932.

11. Carrasquillo, H. F.: Uveitis with Poliosis, Vitiligo, Alopecia and Dysacousia, Arch. Ophth. **28**:385 (Sept.) 1942.

Duke-Elder stated that Harada's disease and chorioretinitis centralis serosa may be related etiologically to the Vogt-Koyanagi syndrome and possibly represent a milder form. The present case, in which there was poliosis and not alopecia or dysacousia, may be an instance of an aberrant form having features common to the two and bridging the gap.

4. As to the cutaneous testing with pigment, Elschnig [12] and Kummel [13] explained sympathetic ophthalmia as an anaphylactic manifestation through sensitization to the uveal pigment. The similarity of Harada's disease pathologically to sympathetic ophthalmia and Vogt-Koyanagi disease suggested the cutaneous testing with uveal pigment. Rones [14] in 1932 performed a like test in 3 cases of Vogt-Koyanagi disease with a positive reaction in 1. It is interesting that Rados' patients and the present one were Italians and the original ones Japanese, persons with much pigmentation.

5. Judging from this and other reported cases in which there has been surgical intervention, it would seem safe to say that affected eyes respond favorably to such intervention.

108 East Sixty-Sixth Street.

12. Elschnig, A.: Arch. f. Ophth. **76**:509, 1910.
13. Kummel, R.: Arch. f. Ophth. **77**:393, 1910; **79**:528, 1911.
14. Rones, B.: Uveitis with Dysacousia, Alopecia and Poliosis, Arch. Ophth. **7**:847 (June) 1932.

EMBRYOLOGY OF MICROPHTHALMOS IN RATTUS NORVEGICUS

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There are a number of influences which affect and arrest the developing eye in its embryonic growth: for example, mechanical injuries, or abnormal pressures; infections, toxicoses, vitamin or other nutritional deficiencies and metabolic and endocrine disturbances in the mother ante partum, and interference with the blood supply to the embryo or to the developing primordia. Certain abnormalities of the eye have been shown to be inherited.

Adelman [1] reviewed literature by Stockard, Guyer and Smith, Little and Bagg and others on the production of ocular abnormalities by artificial means. Hale [2] reported the appearance of such abnormalities in litters from sows reported as deficient in vitamin A. Browman [3] and Cannon [4] were unable to confirm this finding using vitamin A–deficient rats. The problem of cyclopia (Adelman,[1] Wright and Wagner [5]) is not considered to have a direct bearing on the production of microphthalmos in mammals with both eye primordia and optic vesicles already differentiated in the developing embryo.

The spontaneous appearance of microphthalmos in most mammals is well known. Pearson [6] and Reed [7] reported on the appearance of microphthalmos in mice, and similar reports on its appearance in laboratory rats have been made by Hofmann,[8] Jones,[9] Yudkin,[10] King [11] and Hain.[12] The method of inheritance of

1. Adelman, H. B.: The Problem of Cyclopia, Quart. Rev. Biol. **11**:161-182 and 284-304, 1936.

2. Hale, F.: The Relation of Vitamin A to Anophthalmus in Pigs, Am. J. Ophth. **18**: 1087-1092, 1935.

3. Browman, L. G.: The Reproductive Performance of Albino Rats with Previous Vitamin A Depletion Histories, Am. J. Physiol. **125**:335-338, 1939.

4. Cannon, M. D.: Failure of Maternal Vitamin A Depletion to Produce Congenital Anomalies in the Young of Rats, Proc. Soc. Exper. Biol. & Med. **44**:129-132, 1940.

5. Wright, S., and Wagner, K.: Types of Subnormal Development of the Head from Inbred Strains of Guinea Pigs and Their Bearing on the Classification and Interpretation of Vertebrate Monstrosities, Am. J. Anat. **54**:383-447, 1934.

6. Pearson, E. S.: Congenital Eye Anomalies in Albino Mice, Nature, London **114**: 433, 1924.

7. Reed, S. C.: Harelip in the House Mouse: I. Effects of External and Internal Environments, Genetics **21**:339-360, 1936.

8. Hofmann, F. B.: Ueber die Vererbung einer Entwicklungshemmung des Auges bei Ratten, Klin. Monatsbl. f. Augenh. **50**:594, 1912.

9. Jones, E. E.: The Occurrence of an Eye and of a Tooth Abnormality in a Line of Albino Rats, Am. Naturalist **59**:427-440, 1925.

10. Yudkin, A. M.: Congenital Anophthalmos in a Family of Albino Rats, Am. J. Ophth. **10**:341-345, 1927.

11. King, H. D.: Studies on the Inheritance of Structural Anomalies in the Rat, Am. J. Anat. **48**:231-259, 1931.

12. Hain, A. M.: Microphthalmia and Other Eye Defects Throughout Fourteen Generations of Albino Rats, Proc. Roy. Soc. Edinburgh **57**:64-76, 1936.

the defect is not evident in most instances, although Chase [13] reported anophthalmos in a strain of mice to be dependent on one major pair of alleles. Eaton [14] was unable to determine the mode of inheritance of microphthalmos through several generations of guinea pigs. Eaton's illustrations and descriptions of microphthalmos in his guinea pigs fit almost perfectly the anomaly in our strain of rats. Jeffrey,[15] demonstrated that in the domestic fowl microphthalmos is dependent on a simple recessive gene, which induces the abnormality when homozygous.

Numerous reports on human beings with microphthalmos have appeared in the medical literature. In some of these the condition was said to be the result of sex-linked recessive characteristics (Roberts,[16] Fleischer,[17] Iles [18] and Whitnall and Norman [19]), while in others the mode of inheritance was not clear (Rintelen,[20] Mann [21] and Berliner [22]). Adelman,[1] Best,[23] Fleischer [17] and Waardenburg [24] have published extensive reviews of the literature.

From the several reports mentioned and from others, it appears that inhibition of the eye primordia is likely to result in arrest of development of the optic cup and associated structures. The present study on the embryology of microphthalmos in the albino rat was made to uncover the probable cause or causes and to show the development of microphthalmos in a strain of rats in which both optic vesicles appeared in the early embryo.

MATERIALS AND METHODS

Two female rats, one with unilateral and the other with bilateral microphthalmos, appeared in the colony at the Hull Zoological Laboratories, University of Chicago, in 1937. These animals were made available to us. From the mating of the female with bilateral microphthalmos with a normal-eyed litter mate, one microphthalmic animal appeared. Brother-sister matings of this strain were continued in an attempt to increase the proportion of small-eyed animals.

The average percentage of microphthalmic rats increased from a low of 19 to over 85 in the seventh generation (table 1). It is of interest to note that no litter with all animals having some degree of microphthalmos was observed until the seventh generation. In this generation 7 of 20 females produced litters in which all the young exhibited some degree of microphthalmos.

Twenty-two sixth generation microphthalmic females were used in the present investigation to obtain 51 embryos and fetuses. All females had had at least one litter previous to operative recovery of embryos, which gave an indication of the microphthalmic potentialities of each female.

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13. Chase, H. B.: Studies on an Anophthalmic Strain of Mice: III. Results of Crosses with Other Strains, Genetics **27**:339-348, 1942.
14. Eaton, O. N.: A Hereditary Eye Defect in Guinea Pigs, J. Hered. **28**:353-358, 1937.
15. Jeffrey, F. P.: Hereditary Microphthalmia in the Domestic Fowl, J. Hered. **32**:310-312, 1941.
16. Roberts, J. A. F.: Sex-Linked Microphthalmia Sometimes Associated with Mental Deficiency, Brit. M. J. **2**:1213-1216, 1937.
17. Fleischer, B.: Typische Spaltmissbildungen, Mikrophthalmus, Anophthalmus, Aniridie, atypische Kolobome, Kryptophthalmus, in Gütt, A.: Erbleiden des Auges, in Handbuch der Erbkrankheiten, Leipzig, Georg Thieme, 1938, vol. 5, pp. 1-34.
18. Iles, A. E.: Recessive Sex-Linked Blindness, Proc. Roy. Soc. Med. **32**:1614, 1939.
19. Whitnall, S. E., and Norman, R. M.: Microphthalmia and Visual Pathways, Brit. J. Ophth. **24**:229-244, 1940.
20. Rintelen, F.: Zur Morphologie und formalen Genese der Missbildungen bei Mikrophthalmus, Arch. f. Ophth. **135**:120-134, 1936.
21. Mann, I. C.: The Development of the Human Eye, London, Cambridge University Press, 1928.
22. Berliner, M. L.: Unilateral Microphthalmia with Congenital Anterior Synechiae and Syndactylia, Arch. Ophth. **26**:653-660 (Oct.) 1941.
23. Best, H.: Blindness and the Blind in the United States, New York, The Macmillan Company, 1934.
24. Waardenburg, P. J.: Das menschliche Auge und seine Erbanlagen, The Hague, Martimus Nijhoff, 1932.

Pregnant rats received the stock ration (Browman[25]) plus lettuce trimmings and a bread and milk supplement. The estrous cycle was followed by the taking of vaginal smears twice daily. The presence of a vaginal plug or of spermatozoa in the morning smear was considered evidence of insemination. Pregnancy was dated from the midnight previous to the morning smear (Long and Burlingame[26]).

The uterine horns were removed and the embryos dissected out in warm Ringer's solution. Crown-rump measurements and a preliminary determination of ocular anomalies were made with the embryos in the fresh condition. After five hours of fixation in warm Bouin's solution, the embryos were removed, dried by being rolled over twice on filter paper, and weighed.

TABLE 1.—*Number and Percentage of Microphthalmic Rats in the First Seven Generations*

Generation	Normal	Microphthalmic	Total	Percentage Microphthalmic
1	17	11	28	39.3*
2	113	27	140	19.2
3	74	55	129	42.6
4	200	136	336	40.4
5	224	175	399	43.9
6	19	57	76	75.0
7	14	93	107	86.9
Total.....	661	554	1,215	45.5

* Young from one female only.

TABLE 2.—*Time of Appearance of Structural Components of the Rat Eye*

Age in Days	Structural Components
10½	Optic pit
11¼	Closure of neural tube in region of diencephalon; optic vesicle well developed; thickening of surface ectoderm over optic vesicle
11¾	Inauguration of invagination of optic vesicle; lens placode, and inception of lens pit; blood vessels in mesoderm surrounding optic cup
12¼	Invagination of optic vesicle completed; first indication of vascularization via choroid fissure
12½	Lens primordium pinched off from surface ectoderm; two primary retinal layers formed; choroid fissure well developed; hyaloid artery in fissure
13½	Epitrichial cells of lens growing rapidly; annular vessel at rim of cup
14½	Optic stalk narrow but patent throughout; nerve fibers in retina and distal end of optic stalk; primordia of lower eyelids; three distinct layers of retina
15½	Cavity of lens no longer apparent; choroid fissure closed except where hyaloid artery enters cup; optic stalk surrounded by optic nerve; brain contacted by optic nerve; fetal intraocular blood supply well defined; rudiment of choroidal capillaries
17	Lens fibers very distinct; fetal intraocular blood system present; vitreous humor present; upper and lower eyelids growing toward one another but as yet not fused; inception of extrinsic eye muscles; five layers of inner wall of optic cup
18	Rudiment of anterior chamber; vascular mesenchymal tissue in association with anterior surface of lens; vascularization of posterior surface of lens by hyaloid arterioles; vascularization of choroid well established; eyelids fused; lacrimal glands, plica semilunaris and nasolacrimal duct present; extrinsic ocular muscles organized as distinct muscles
21	All basal layers of adult eye present; initiation of iris, anterior chamber, canal of Schlemm, sclera, cornea; retrogression of fetal intraocular blood system in initial stages; primordia of eyelashes; sweat glands and oil glands

OBSERVATIONS

The development of the normal eye in a series of embryos from microphthalmic females was followed from the optic vesicle stage (eleven days) to the stage just before delivery (twenty-one days from insemination). Table 2 indicates in chronologic order the approximate time of the initiation of the different structures of the normal optic apparatus in this strain.

25. Browman, L. G.: The Effect of Optic Enucleation on the Male Albino Rat, Anat. Rec. **78**:59-77, 1940.

26. Long, J. A., and Burlingame, P. L.: The Development of the External Form of the Rat with Observations on the Origin of the Extraembryonic Coelom and Foetal Membranes, Univ. California Publ., Zoöl. **43**:143-184, 1938.

No abnormalities in the development of the optic primordia were evident during the optic placode stage or during the formation of the optic vesicle. No histologic differences were observed between the prospectively microphthalmic and the prospectively normal eyed in a series of embryos taken between the ages of 8½ and 11 days. Embryos approximately 11¼ days of age exhibited only minor variations

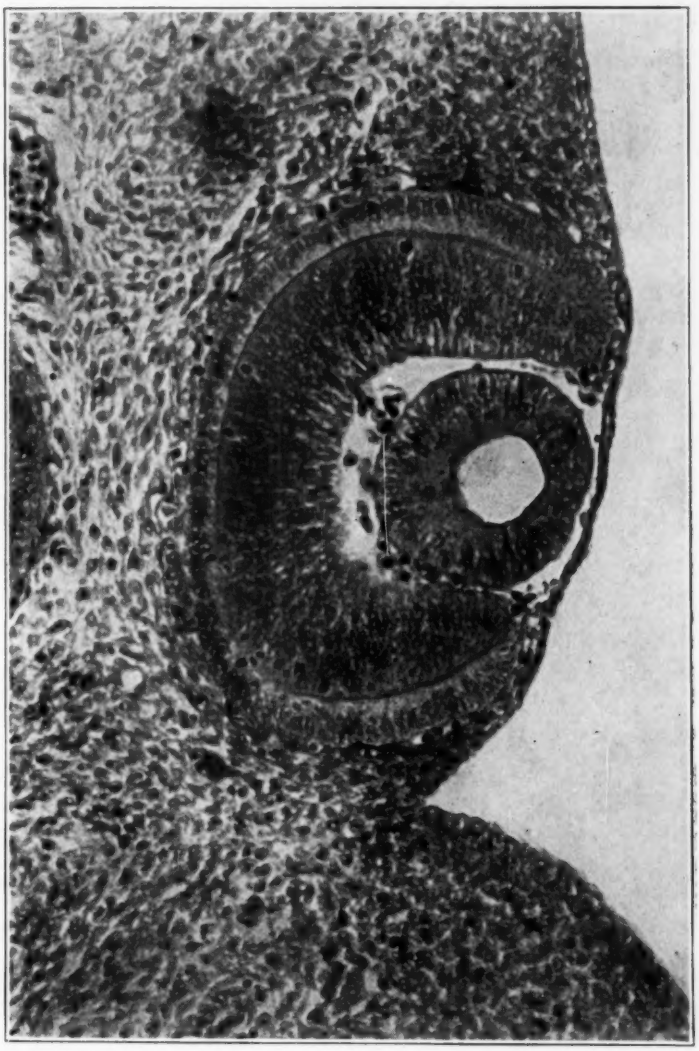

Fig. 1.—Photomicrograph of a longitudinal section of normal eye from embryo 1, female 699; approximate age, 13 days (× 133 before reduction).

in measurements. The optic vesicle was well formed, and no aberrations in structure were observed.

Embryos of approximately 12 and 12¼ days showed invagination of the optic vesicle at the lateral bulge. The coaptation and adhering of the lens placode to the developing cup indicates the intimate relationship that exists at this stage between

the retinal layer and the lens (Ballard [27]). Thus far little differentiation in the retinal layers had occurred.

Arrested development of the eye was first seen in an embryo approximately 12½ days old. The aberration had occurred in the retinal layer and was associated with a retarded invagination of the optic vesicle, which resembled a flattened,

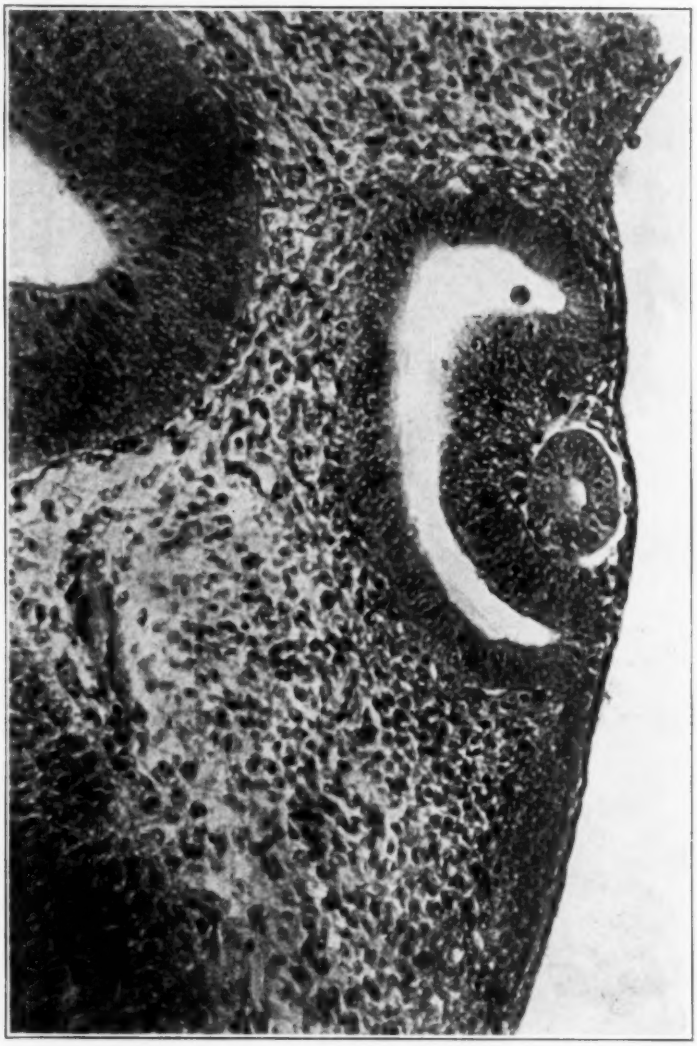

Fig. 2.—Photomicrograph of a longitudinal section of a slightly microphthalmic eye from embryo 3, female 699, showing an early arrest in the development of the eye; approximate age, 13 days (× 133 before reduction).

collapsed balloon. The choroid fissure had developed normally, but there was no evidence of the hyaloid artery or other blood supply via the choroid fissure, although litter mate embryos with normal optic vesicles did have hyaloid arteries. The lens was smaller than the lenses of normal litter mates. It is well known that the retina

27. Ballard, W. W.: Mutual Size Regulation Between Eyeball and Lens in Amblystoma, J. Exper. Zool. **81**:261-285, 1939.

controls the size of the lens. Ballard [27] showed in amblystoma that there is a mutual size regulation between the eyeball and the lens.

The hyaloid artery was missing from the choroid fissure and from the invaginated optic cup in a microphthalmic rat at 13 days. (Compare figure 2 with figure 1, which shows a normal eye.) This blood vessel and any other blood supply via the choroid fissure appeared to be missing in every microphthalmic embryo

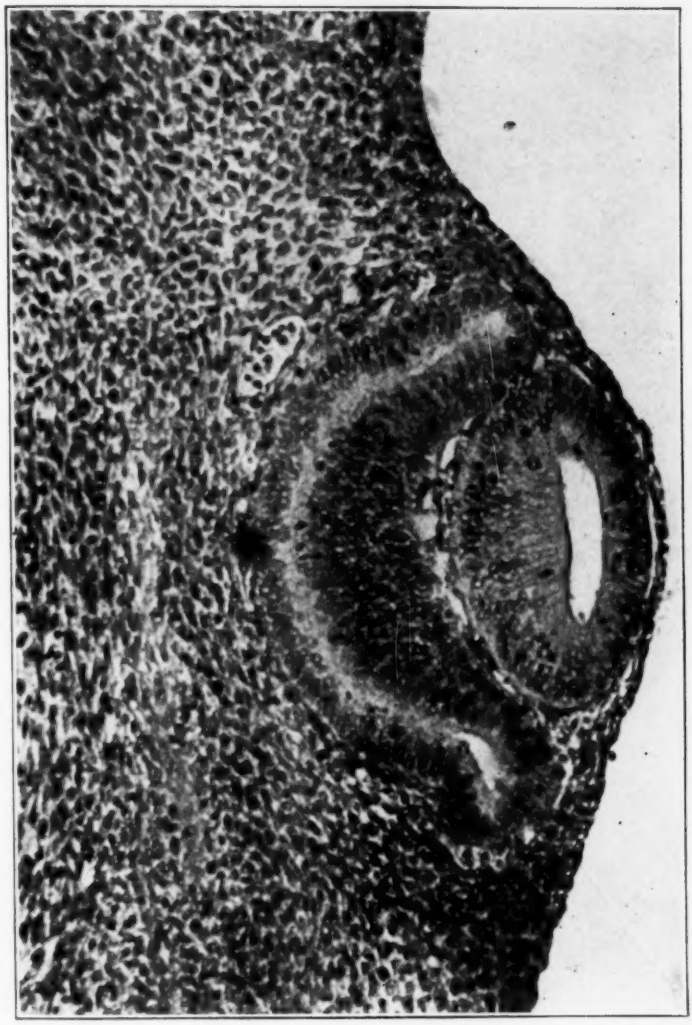

Fig. 3.—Photomicrograph of a longitudinal section of a microphthalmic eye from embryo 1, female 654, showing a severe degree of arrested development; approximate age, 13 days and 13 hours (× 133 before reduction).

examined. The lens of the embryo was approximately one-half the size of the lens of a normal litter mate. There was persistence of undifferentiated mesenchyme in the regions between the lens and the retina.

Another embryo showing arrested development at 13½ days had a normal optic stalk but a deformed optic cup. Consequently there was no intimate association between the lens and the optic cup, and the lens was lying outside the cup proper.

There was no hyaloid artery present. Abnormalities of histologic structures in the retina were apparent (fig. 3). Only one zone (three nuclear layers in thickness) could be seen in the inner layer of the optic cup, as compared with the definite internal limiting membrane, the marginal layer (free from nuclei) and the deeper zone of from seven to nine layers of elongated nuclei of a normal litter mate.

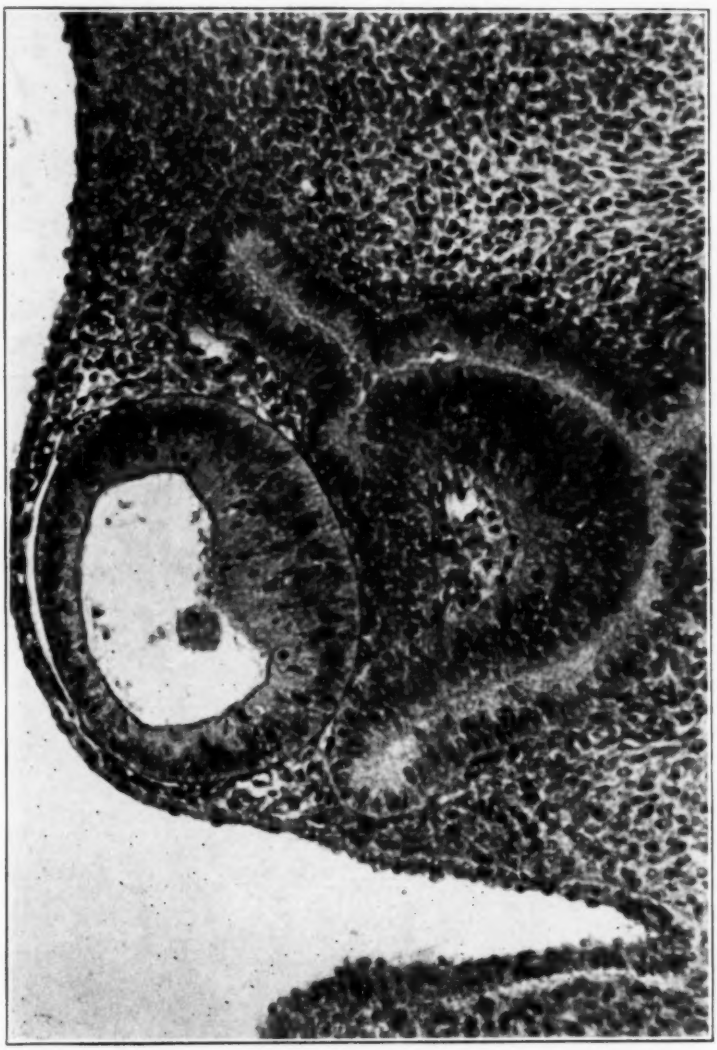

Fig. 4.—Photomicrograph of a longitudinal section of a microphthalmic eye from embryo 8, female 618, showing a severe degree of arrest in growth of the optic cup and lens; approximate age, 14 days and 12 hours (× 133 before reduction). Note the malformation of the optic cup and the failure of migration of nuclei and elongation of cells in the posterior wall of the lens.

Lateral mesenchymal infiltration between the lens and the optic cup persisted, but this condition was not apparent in the optic cup of normal embryos of the same age.

Both the lens and the optic cup of one eye were defective in an embryo of 14½ days, and there was no evidence of a hyaloid artery. The lens and optic cup were smaller than those of the other eye, which was normal; differentiation had not taken place normally, and development had been markedly retarded (fig. 4).

Although arrest in development of the lens had occurred, complete arrest had not taken place, for the nuclei of the posterior wall had started to migrate anteriorly toward the lens cavity. There was no elaboration of the nervous layer of the retina of the optic cup into specialized cells or layers. Nerve fibers in the optic cup of a normal litter mate were developing from the cells of the inner layer of the cup and were migrating along the distal end of the optic stalk, but no nerve fibers were detected in the microphthalmic eye.

The internal carotid artery on the side of the microphthalmic eye was approximately one-half the size of that on the opposite side, which vascularized the normal eye. The annular blood vessels, or a plexus of blood vessels around the rim of the

TABLE 3.—*Measurements from Selected Embryos of the Microphthalmic Strain*

Age in Days	Crown-Rump, Mm.	Weight, Mg.	Number of Sections Through Eyeball	Lens at Optic Axis, Microns	Section Cut at Right Angles to Optic Axis Through Optic Cup, Microns	Nervous Layer of Retina to Optic Axis, Microns
12½	6.6	35	34	160	346	69
			33	168	388	79
12½	7.0	25	28*	69	282	57
			33*	112	228	67
13	...	..	31	132	336	75
			34	134	337	75
13	...	..	32*	93	337	75
			27*	56	300	68
13½	8.5	67	38	163	448	88
			42	187	459	99
13½	8.5	65	36*	121	337	79
			32*	159	335	78
14½	11.0	146	68	262	562	112
			65	263	573	120
14½	11.0	156	46*	225	375	112
			46*	245	412	96
15½	13.2	260	76	375	750	150
			76	337	768	150
15½	12.2	186	43*	187	233	18
			32*	111	203	..
16¾	15.1	420	86	337	731	170
			36*	190	338	14
18½	23.4	1,286	125	525	1,215	150
			49*	236	432	15
20¾	38.0	3,970	196	1,087	2,324	225
			128*	712	1,425	187
20¾	37.0	3,630	20*	309	337	...
			43*	300	487	18

* Microphthalmos; the first measurements are of the left eye.

cup, had formed in the normal eye, but only a few vessels were present at the rim of the cup of the microphthalmic eye.

One animal at 14½ days showed what was interpreted to be a slight bilateral microphthalmic condition. Both of the optic cups were smaller than those of a normal litter mate and slightly malformed, although the layers were essentially normal in appearance. Differentiation and development of the cells of the posterior wall of the lens had been retarded. No hyaloid artery could be found in either eye, and the optic cup appeared to be receiving its blood supply only through a plexus of annular blood vessels. It is probable that this animal as an adult would have had two eyes that appeared normal but would have been smaller and nonfunctional because the optic nerve would have failed to develop. It was often observed at autopsy in this microphthalmic strain that rats with apparently normal eyes lacked an optic nerve.

The complete lack of either a hyaloid artery or an annular blood supply to the optic cup was associated with a severe microphthalmic condition in a 15½ day old embryo (fig. 5). A sheath of mesenchyme completely encircled the spherical lens and filled the rest of the cup. The lens was approximately one-half the size of the normal lens of a litter mate. The lens cavity was partially filled with sloughed-off

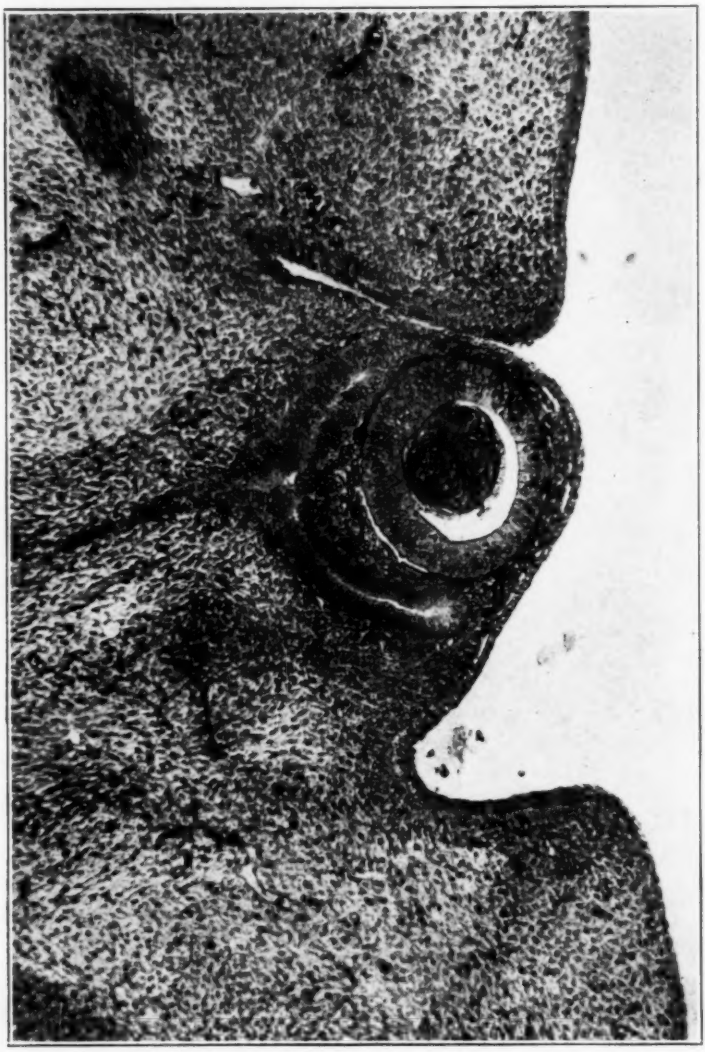

Fig. 5.—Photomicrograph of a longitudinal section of a microphthalmic eye from embryo 11, female 651, showing severe arrested development; approximate age, 15 days and 12 hours (× 76.5 before reduction). Note the invasion of mesoderm into the optic cup and the unorganized material in the lens cavity.

lens material, while in the normal lens at this time the cavity was obliterated by the growth of the posterior wall cells. The optic cup consisted of a pars optica and pigment layers that were almost identical in thickness and in the type of cells. Each was composed of two or three layers of nuclei in which initial stages of cytolysis

were evident. No evidence of an optic nerve or nerve fibers was found, although in a normal-eyed litter mate the fibers of the optic nerve had made contact with the brain.

Only 2 brain anomalies associated with microphthalmos were observed in this series. Figure 6 represents severe microphthalmos associated with an almost complete lack of brain ventricles and a collapsed optic stalk. This lack of cephalic

Fig. 6.—Photomicrograph of a longitudinal section of a microphthalmic eye from embryo 7, female 651; approximate age, 15 days and 12 hours (× 76.5 before reduction). Note the primordium of the upper and of the lower eyelid.

lumens may have been the result of an absence of intracerebral fluid, with a subsequent collapse of the brain walls. The second brain anomaly occurred in a microphthalmic fetus approximately 17 days of age. The brain walls approached each other, with a consequent reduction in the size of the brain ventricles. There was no detectable evidence of either optic stalk or optic nerve. Roberts [16] and

Kallman, Barrera and Metzger [28] reported on the association of microphthalmos with mental deficiency in human beings.

In some microphthalmic eyes nerve fibers from the cells of the inner layer of the retina failed to develop. In others the nerve fibers arose from the ganglion cells of the retina but pierced the nervous layer of the retina near the rim at the lower or upper part of the cup instead of emerging from the base of the cup at the

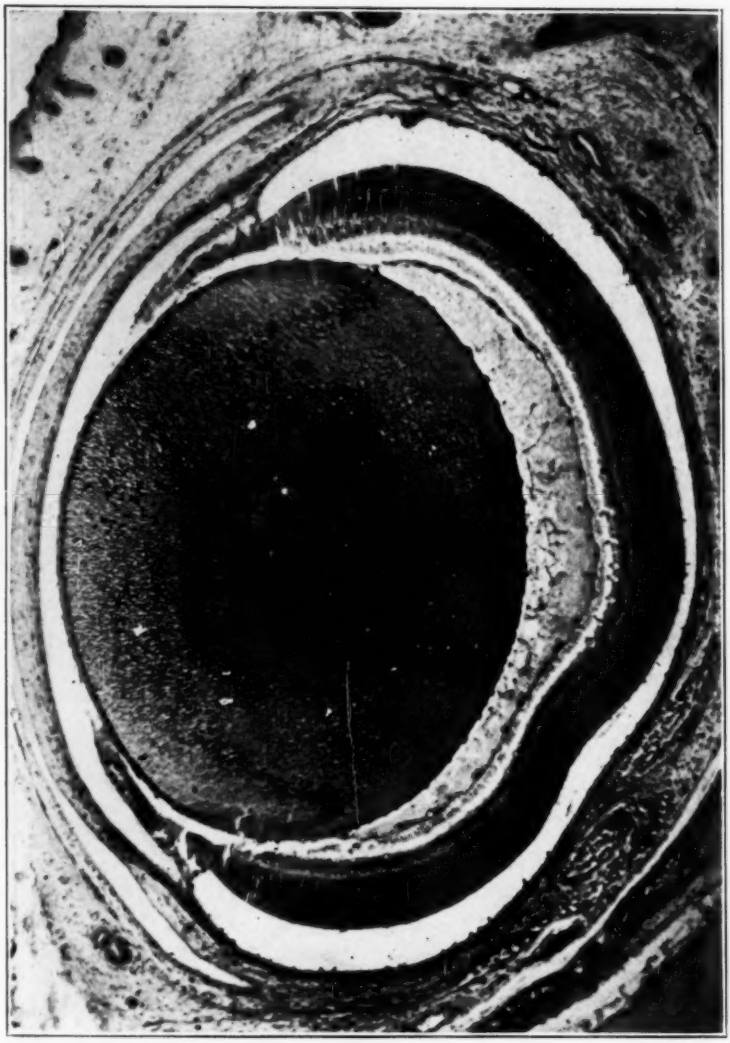

Fig. 7.—Photomicrograph of a longitudinal section of a normal eye from embryo 10, female 640. Approximate age, 20 days and 21 hours (× 34.5 before reduction). Note the formation of the cornea, anterior chamber, extrinsic eye muscles, lacrimal gland, vitreous humor and primordium of the iris.

optic stalk. Frequently if the fibers did emerge from the cup at the optic stalk, they did not continue to follow the stalk but wandered aimlessly from it.

28. Kallman, F. J.; Barrera, S. E., and Metzger, H.: Association of Hereditary Microphthalmus with Mental Deficiency, Am. J. Ment. Deficiency **45**:25-36, 1940.

Autopsy disclosed that the optic nerves were missing in 19 of 48 adult rats which had apparently normal-sized eyes, with no opacities or other abnormalities. The peculiar condition of absence of the hyaloid artery with a well developed annular blood supply probably accounts for the appearance of a normal eyeball without an optic nerve, as well as for different degrees of microphthalmos in this strain. Scheie and Adler [29] reported that both eyes were present and well developed

Fig. 8.—Photomicrograph of a longitudinal section of a microphthalmic eye from embryo 12, female 640, showing a severe arrested development; approximate age, 20 days and 21 hours (× 34.5 before reduction). Note the degeneration of the tissue of the lens and optic cup.

in the absence of both optic nerves in a 3 year old child. Matthews,[30] in Fundulus destroyed the optic nerve but left the blood supply to the retina intact and found little if any change in the retina.

29. Scheie, H. G., and Adler, F. H.: Optic Aplasia, Arch. Ophth. **26**:61-70 (July) 1941.
30. Matthews, S. A.: Changes in the Retina of Fundulus After Cutting the Optic Nerve and the Blood Vessels Running to the Eye, J. Exper. Zool. **66**:175-192, 1933.

A variation in the expression of severity of microphthalmos was seen in the several embryos examined at the age of 17 days. No vitreous humor was present in severely microphthalmic eyes, though there was abundant evidence of it in the normal eyes. The eyelids of both normal and microphthalmic animals were fused at this stage, a fact indicating that the arrest in the development of the optic cup had not affected the growth of the eyelids. The differentiation and development of the lens had been interfered with in various ways. Lens material within the cavity often showed large vacuoles, pyknotic cells and a disorganized scattering of apparently disintegrating cells. The anterior wall cells were often identical with those cells of a normal lens of the same age, but the posterior wall cells were already showing signs of disorganization. A concentration of mesodermal tissue around the orbit showed that the development of extrinsic ocular muscles was proceeding normally.

The several microphthalmic embryos studied between the seventeenth and twenty-first days showed severe retardation of the optic apparatus, but the anomalies were essentially repetitions of those already described (fig. 8). As would be expected, all severe conditions of early arrest in development of the eye (optic cup and lens) resulted in failure of the normal development of the choroid, sclera, cornea and iris. The lacrimal gland and extrinsic ocular muscles were present in the orbit, but the defective condition of the eye had distorted their growth and relationship to the eyeball. (Compare figure 8 with figure 7, which shows a normal eye of the same age.)

COMMENT AND SUMMARY

Differences between normal and microphthalmic eye primordia could not be detected during the formation of the optic fovea and out-pocketing of the lateral wall of the diencephalon (approximately 11¼ days). It is well known that proliferation and growth of cells in an embryo can continue up to a certain stage without a definitive blood supply. Beyond this critical point in development, a source of nourishment to accompany normal differentiation and growth of cells and tissues is essential. The lack of normal development in the lens primordium and optic vesicle was first seen at about 12½ days, when the cells of the posterior wall of the lens failed to elongate and differentiate and the optic vesicle first showed evidence of retarded development. It is at this time that the hyaloid artery is definitely established in the choroid fissure in the rat. The optic cup and posterior face of the lens receive their major embryonic blood supply from this source. In none of the 10½ to 12 day old embryos studied did the optic vesicle and the optic cup reveal abnormalities. Therefore it would seem that the critical period in the formation of microphthalmos in this strain of rats is at the time of formation of the embryonic blood supply to the eye, at 12 to 13 days.

Chase and Chase,[31] found in their strain of anophthalmic mice that the critical stage was during the formation of the optic cup. Cairns [32] and Gayer [33] found that deficient circulation to the forebrain and midbrain in homozygous creeper embryos induced developmental abnormalities and asymmetries of the optic cup, lens vesicles, etc., with death occurring on the third day.

The lack of an adequate blood supply and the absence of a hyaloid artery or a tunica vasculosa retinae in all the defective eyes examined in this study emphasize

31. Chase, H. B., and Chase, E. B.: Studies on an Anophthalmic Strain of Mice: I. Embryology of the Eye Region, J. Morphol. **68**:279-301, 1941.

32. Cairns, J. M.: The "Early Lethal" Action of the Homozygous Creeper Factor in the Chick, J. Exper. Zool. **88**:481-503, 1941.

33. Gayer, K.: A Study of Coloboma and Other Abnormalities in Transplants of Eye Primordia from Normal and Creeper Chick Embryos, J. Exper. Zool. **89**:103-133, 1942.

their importance during the early stages of ocular development. During early differentiation the optic cup and lens in the rat depend on receiving their intraocular blood supply largely by way of the hyaloid artery. It is evident that the lack of a hyaloid artery results in failure of development of the retina and subsequently of the vitreous body. If the hyaloid blood system develops normally, a normal cup and eye result, but if there is a failure in the development of the hyaloid system, microphthalmos results. The slightly microphthalmic eye and lens receive most of their blood supply from the anastomosing annular system around the rim of the optic cup. Differentiation and development of their tissue are retarded, but not as greatly as those of the severely microphthalmic eye. Mann [34] and Lyle [35] described changes associated with the development of abnormal eyes in human embryos.

It was observed that differentiation of the lens and elaboration of the nervous layer of the retina into specialized cells and layers did not occur in instances of severe microphthalmos. The lens cavity in the late fetal stage is usually partially or entirely filled with sloughed-off lens material. Large vacuoles in the lens are characteristic of less severe retardation. Initiation of nerve fibers from the inner nervous layer of the retina was noted in the normal eye by 14½ days, but this was never found in severe microphthalmos. Eyes that exhibited minor arrests in development had nerve fibers which had not contacted the brain by way of the optic stalk, as they do in the normal eye, by 15½ days.

Extrinsic ocular muscles were present in all microphthalmic eyes of older embryos but had not developed to the same extent as those of normal-eyed litter mates. Accessories of the eye such as eyelids, the lacrimal glands and the nasolacrimal duct did develop, but their relationship with the eyeball was distorted by the disorganization of the optic cup. Development of eyelashes, sweat glands and oil glands occurred in all the fetuses studied. However, in severely microphthalmic eyes well differentiated choroid, sclera, cornea and iris were not found.

Department of Zoology, Montana State University, Missoula, Mont.

Dawson County Junior College, Glendive, Mont.

34. Mann, I. C.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937.

35. Lyle, D. J.: Arrests in Embryonic Development as Factors in Vision, Arch. Ophth. **21**:1037-1054 (June) 1939.

APPLICATION OF WETTING AGENTS IN OPHTHALMOLOGY

WITH PARTICULAR REFERENCE TO SULFONAMIDE COMPOUNDS

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It has been shown that the sulfonamide compounds with the exception of sulfanilamide penetrate the cornea poorly.[1] Judging from the findings of Swan and White,[2] we may assume that this poor penetration is due to the polar nature of the drugs. Further, the concentrations reached in the ocular tissues and fluids when sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole), sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) and sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) are administered orally or locally fall short of the values believed to be necessary for therapeutic effectiveness.

Boyd[3] and von Sallmann,[4] using sulfathiazole and sulfadiazine, respectively, increased the penetration through the cornea by means of iontophoresis. With this method the concentration of the drugs in the corneal tissues and aqueous humor increased three to fifteen times over the values obtained with the corneal bath alone.

One of us (J. B.[5]) recently mentioned that a marked increase in the penetrability of the sulfonamide compounds may be obtained through the use of a wetting agent.

It is not our purpose to present here a review of the literature on wetting agents, but merely to state the action of these agents and to direct the attention of ophthalmologists to their possible usefulness. The general interest in this subject is demonstrated by the fact that over a thousand patents have been issued for compounds possessing wetting properties.[6]

A wetting agent is defined as a substance which by lowering interfacial tension increases penetration and acts as a detergent or emulsifying agent or in some

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1. Bellows, J., and Chinn, H.: Penetration of Sulfathiazole in Eye, Arch. Ophth. **25**: 294 (Feb.) 1941. Chinn, H., and Bellows, J.: J. Lab. & Clin. Med. **25**:735, 1940; Corneal Penetration of Sulfanilamide and Some of Its Derivatives, Arch. Ophth. **27**:34 (Jan.) 1942. Scheie, H. G., and Leopold, I. H.: Penetration of Sulfathiazole into Eye, ibid. **27**:997 (May) 1942. Scheie, H. G., and Souders, B. F.: Penetration of Sulfanilamide and Its Derivatives into Aqueous Humor of Eye, ibid. **25**:1025 (June) 1941. Meyer, K.; Block, H. S., and Chamberlain, W. P., Jr.: Am. J. Ophth. **24**:60, 1941. Lou, T. H., and P'an, S. Y.: Chinese M. J. **58**:167, 1940. Mengel, W. G.: Determination of Sulfanilamide in Aqueous and Vitreous After Conjunctival and Oral Administration, Arch. Ophth. **22**:406 (Sept.) 1939. Guyton, J. S.: Am. J. Ophth. **24**:292, 1941.

2. Swan, K. C., and White, N. G.: Am. J. Ophth. **25**:1043, 1942.

3. Boyd, J. L.: Sodium Sulfathiazole Iontophoresis, Arch. Ophth. **28**:205, 1942.

4. von Sallmann, L.: Sulfadiazine Iontophoresis for Bacillus Pyocyaneus Infection of Rabbit Cornea, Arch. Ophth. **29**:690 (April) 1943.

5. Bellows, J.: Chemotherapy in Ophthalmology, Tr. Am. Acad. Ophth. **47**:19, 1942.

6. Duemling, W. W.: Wetting Agents, Arch. Dermat. & Syph. **43**:264 (Feb.) 1941.

other way manifests surface activity. It consists of molecules containing a polar and a nonpolar group. As a result the molecules concentrate on the surface of the cornea and orient themselves so that the polar group is in contact with the epithelium and the nonpolar portion is directed outward to the surrounding media. Consequently, the interfacial tension between the surrounding media and the epithelium is decreased, bringing about an increased penetration of both the wetting agent and other substances which would not by themselves penetrate readily. Incidentally, wetting agents have been shown to possess bactericidal powers.

O'Brien and Swan,[7] using carbaminoylcholine chloride and a 1:3,000 solution of zephiran (a mixture of high-molecular alkyl, dimethyl and benzyl ammonium chlorides), which has relatively little wetting power, found that better results are obtained than when carbaminoylcholine chloride is used alone. Gifford [8] has suggested that wetting agents might be of value in the treatment of keratitis sicca, since their presence would increase the moistening effect of the usual slight amount of tears. Conceivably, wetting agents may make the more generally used surface antiseptics, for example metaphen, more penetrating and effective. Investigation is under way to determine the effect of wetting agents combined with the more generally used ophthalmologic drugs, such as miotics, mydriatics and surface anesthetics. It is probable that the combination would increase the effectiveness of these drugs. In this particular investigation we attempted to determine whether the concentration of sulfonamide compounds in the ocular fluids and tissues could be increased by means of wetting agents to such an extent as to fall well within the range of chemotherapeutic effectiveness. In addition we wished to test some of the more readily available commercial preparations for their applicability to clinical use.

EXPERIMENTS

Young adult rabbits were used in our investigation. The wetting agents used, their chemical structure and their manufacturers are shown in table 1.

The sulfonamide compounds employed were sulfanilamide, sulfathiazole, sulfadiazine and sulfapyridine.

To approximately 100 mg. of the sulfonamide compound a sufficient amount of the wetting agent to be tested (about 5 drops) was added to make a paste. The paste was applied to the cornea and conjunctival sac, and the lids were massaged lightly over the eyeball to distribute the drug. Throughout the time of the experiment (usually ninety minutes) particular care was taken to keep a large amount of the substance in the conjunctival sac. At the end of this period the cornea and conjunctiva were subjected to a thorough irrigation to remove all traces of the paste. The aqueous humor was then aspirated and analyzed for the content of the sulfonamide compound, Marshall's method [9] being used. In many instances the content of the drug in the lens, vitreous, uvea and retina and cornea and sclera was determined by the method described by Bellows and Chinn.[10]

To obtain control values, a paste made by adding water to the drug was introduced into the second eye. In most instances sulfathiazole was used for comparing the effectiveness of different wetting agents, because by itself it penetrates the cornea very poorly. (Values from 0.5 to 2 mg. per hundred cubic centimeters were found for the aqueous.)

As table 2 indicates, all the wetting agents caused an increased penetration of sulfathiazole. Since we did not have zephiran in a concentration higher than 1:1,000, its effect in higher concentrations was not determined. Since aerosol OS

7. O'Brien, C. S., and Swan, K. C.: Carbaminoylcholine Chloride in Treatment of Glaucoma Simplex, Arch. Ophth. **27**:253 (Feb.) 1942.

8. Gifford, S. R.: Personal communication to the authors.

9. Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**:539, 1939.

10. Bellows, J., and Chinn, H.: Distribution of Sulfanilamide in Eye, J. A. M. A. **112**: 2023 (May 20) 1939.

causes no irritation and we obtained good, consistent results with a 0.5 per cent concentration, and since this wetting agent is stable both in acid and in alkaline mediums, it was chosen as the constant factor in the comparison of the corneal penetration of various sulfonamide compounds. The results are shown in table 3. As can be seen, the use of a wetting agent increases penetrability two to fifteen times.

Next, the effect of different concentrations of wetting agents on the penetration of sulfathiazole was studied. Typical results with aerosol OS are shown in chart 1. The values obtained with aerosol OT were somewhat lower than those obtained

TABLE 1.—*Wetting Agents Used in the Experiments*

Name	Chemical Structure	Manufacturer
Aerosol OT	Dioctyl ester of sodium sulfosuccinate	American Cyanamid and Chemical Corporation
Aerosol OS	Isopropyl naphthalene sodium sulfonate	American Cyanamid and Chemical Corporation
Tergital, 4, 7	Higher secondary alcohol sulfate	Carbide and Carbon Chemicals Corporation
Tergital OS	Synthetic primary alcohol sulfate	Carbide and Carbon Chemicals Corporation
Ocenol KD	Oleyl alcohol	E. I. Du Pont de Nemours & Co., Inc.
Sodium lauryl sulfate		
Zephiran	High-molecular alkyl, dimethyl and benzyl ammonium chlorides	Alba Pharmaceutical Co., Inc.

TABLE 2.—*Effect of Various Wetting Agents on the Penetration of Sulfathiazole*

Wetting Agent	Sulfathiazole in Aqueous, Mg. per 100 Cc.
Aerosol OT 1%	11.3
Aerosol OS 1%	14.8
Sodium lauryl sulfate 1%	8.1
Tergitol 7 1%	5.6
Ocenol KD (with sulfathiazole jelly [Abbott])	7.4
Zephiran 1:1,000	1.4
Bile salts 5%	20.0

TABLE 3.—*Effect of 0.5 Per Cent Aerosol OS on the Penetrability of Various Sulfonamide Compounds*

Drug	Concentration in Aqueous, Mg. per 100 Cc.	
	Control Eye	Eye with Wetting Agent
Sulfanilamide	9.1	20.8
	13.2	23.5
Sulfapyridine	0.6	5.0
	0.9	2.5
	....	6.8
Sulfadiazine	1.0	4.5
	....	7.0
	....	1.6
Sulfathiazole	0.5 to 2	14.2
	....	16.3

with aerosol OS. The effects of different concentrations of tergitol 7 are shown in table 4.

We next conducted a group of miscellaneous experiments to determine the effect of other factors superimposed on the influence of the wetting agents in conjunction with the sulfonamide compounds.

Local heat applied with a lamp was maintained at a temperature of 55 C. in the immediate vicinity of the eyeball. An increase in systemic heat was produced by placing the animals in a room heated to 45 C. during the time of the experiment.

Both forms of heat caused a threefold increase (to 5 to 6 mg. per hundred cubic centimeters) in the concentration of drug in the aqueous humor of the

control eyes. In the eyes treated with wetting agents the already high value for the penetration of sulfathiazole was increased with local heat by 50 per cent (20 mg. per hundred cubic centimeters) and with systemic heat by 75 per cent (26 mg.).

The influence of vasodilation produced by inflammation following infection with hemolytic streptococci in the vitreous chamber or by injection of mecholyl chloride and histamine was also studied.

Like heat, infection caused a threefold increase in the penetration of sulfathiazole in the control eyes (concentration in the aqueous, 6 mg. per hundred cubic centimeters), whereas with wetting agents the already high penetration was increased by about 50 per cent (concentration in the aqueous, 20 mg.).

Histamine and mecholyl chloride caused some increased penetration. The concentrations of the sulfonamide compounds, with the exception of sulfanilamide, attained in the lens, vitreous, uvea and retina were in all instances, with or without a wetting agent, below 1 mg. per hundred grams of moist tissue. In the cornea

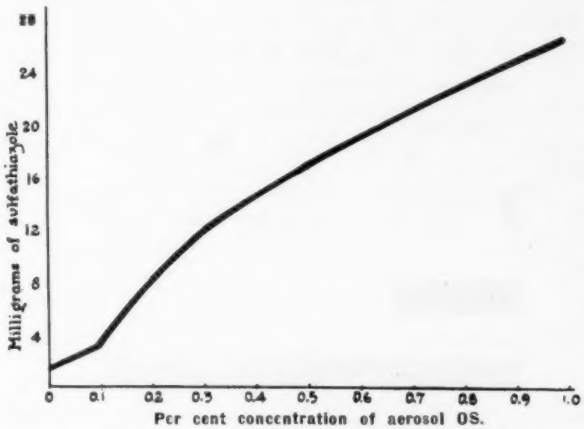

Chart 1.—Curve showing the increase in the penetration of sulfathiazole with rising concentrations of aerosol OS.

TABLE 4.—*Effects of Different Concentrations of Tergitol 7 on the Penetration of Sulfathiazole*

Percentage Concentration of Tergitol 7	Sulfathiazole in Aqueous Humor, Mg. per 100 Cc.
0.5	1.4
1.0	5.6
5.0	7.4
10.0	10.6
Undiluted	17.0

and sclera the concentration was generally high, well above therapeutically effective values, and was somewhat higher when a wetting agent was used.

COMMENT

All the wetting agents caused a marked increase in the concentrations of the sulfonamide compounds in the aqueous humor, so that they reached a point above that considered necessary for chemotherapeutic effectiveness. Thus a simple means

is at hand for increasing the concentration of these drugs in the cornea and aqueous, making the more complicated method of iontophoresis unnecessary. Zephiran was used only in the form readily available, a concentration of 1 : 1,000; so the results obtained with this agent are not comparable to the values noted with other wetting agents in much higher concentrations. It was shown that the penetration increases as the concentration of the wetting agent rises. With aerosol OS a concentration of at least 0.2 per cent is required to obtain a significant penetration, and a 10 per cent concentration produces a penetration approaching saturation.

Aerosol OS in solutions of 1 per cent or less produces no sign of irritation or damage to the conjunctiva or cornea. Signs of irritation are noted with solutions above 2 per cent, increasing with the concentration. With 5 to 10 per cent solutions the cornea becomes hazy. However, the effect is transient, for the cornea is found to be clear the following day.

Since significantly increased penetration occurs with solutions of aerosol OS ranging from 0.3 to 0.5 per cent, the margin of safety is satisfactory for clinical purposes. Roughly the same findings hold true for other wetting agents (the tergitols and aerosol OT).

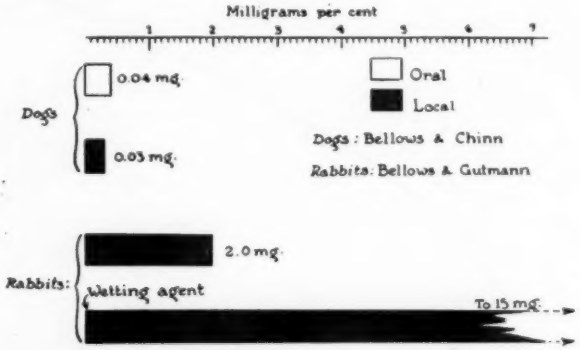

Chart 2.—Concentration of sulfathiazole in the aqueous humor with oral and with local administration.

It appears that in the case of sulfanilamide, which by itself penetrates more readily than the other agents, the increase noted is not of great practical significance. On the other hand, with sulfathiazole, sulfapyridine and sulfadiazine, which by themselves penetrate poorly, a wetting agent is essential in bringing about a therapeutically effective concentration. Sulfathiazole, which is used so widely, shows even more than the other drugs tested the remarkable effectiveness of wetting agents. This effectiveness was noted even in the cornea of a dead rabbit. With the exception of the cornea and sclera, the slight increase in the ocular tissues fell short of the therapeutically active values. A possible explanation of the low values in the vitreous and consequently in the other tissues of the posterior segment is the ball-valve effect of the lens and iris.

Local and general heat affect the penetration of the drugs favorably, indicating another good reason for the common clinical practice of raising local and systemic temperature in the treatment of ocular infections.

These studies show that a higher concentration of the sulfonamide compounds in the anterior chamber of the eyeball can be expected from the use of these drugs with wetting agents than from oral administration (chart 2). Because usually other tissues are involved in infections of the anterior segment, better results may

be expected if local application in conjunction with a wetting agent is combined with oral administration. For infections involving the posterior segment, one is dependent solely on oral administration.

SUMMARY AND CONCLUSIONS

Certain of the more common wetting agents (aerosol OT; aerosol OS; tergitol 4, 7 and 08; ocenol KD; sodium lauryl sulfate, and zephiran) were applied to the eyeballs of rabbits with no obvious untoward effects when used in the recommended concentrations.

These agents considerably increased the penetration of the sulfonamide compounds (with the exception of 1:1,000 zephiran solution).

Minimal concentrations of aerosol OS, aerosol OT and the tergitols, ranging from 0.25 to 1 per cent, are required to produce an effective increase in corneal penetration.

The influence of wetting agents in increasing corneal penetration was demonstrated, particularly in the case of sulfathiazole, probably the most widely used sulfonamide compound.

The action of local and systemic heat and inflammation, with their attendant vasodilatation, superimposed on the influence of the wetting agent causes an even greater penetration.

In conclusion, a simple method of obtaining chemotherapeutically effective levels of the sulfonamide compounds for combating infections of the anterior segment of the eyeball is application in the presence of a suitable wetting agent. Since the adjacent tissues frequently participate in these infections, optimum results are to be expected from a combination of oral administration with local application in conjunction with a wetting agent.

Prof. S. R. Gifford gave advice on this work.

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LIPAEMIA RETINALIS

REPORT OF A CASE

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Lipaemia retinalis is of sufficient rarity to warrant the contribution of this report to the medical literature. A careful survey indicates that the case is the sixty-second to be reported since Heyl's [1] original article, published in 1880.

Lipaemia retinalis, with 2 exceptions, has appeared in cases of diabetes mellitus and has been accompanied by a state of acidosis. The majority of the patients were either in or on the verge of coma when first seen. The condition is predominantly a disease of young diabetic patients, rarely being found in patients over 30.

An increase in plasma lipid is associated with a large variety of clinical entities: pneumonia, peritonitis, alcoholism, phosphorus poisoning, asphyxia, starvation, xanthomatosis, carcinoma, tuberculosis and trench nephritis. It is only in diabetes mellitus, as a rule, that the plasma lipid becomes emulsified in sufficient quantity to be seen in the blood stream with the aid of the ophthalmoscope. The exceptions which have been noted were in a case of leukemia treated by intensive irradiation reported by Wagener [2] and in a case of acromegaly complicated by diabetes.[3] The lipaemia retinalis and the visual acuity in the latter case responded satisfactorily to roentgen ray therapy and administration of insulin. It is now accepted that an increase in the plasma lipid is not in itself sufficient to produce retinal lipemia; an emulsification of the lipid is necessary. Some authors maintain that an anatomic change of the vessels effecting a change in permeability is also a requisite. To date no known explanation or physiologic mechanism has been proposed which accounts for this modification of the physical state of the plasma lipid. Acidosis is necessary to the phenomenon of emulsification. The reported level of blood lipid necessary to the appearance of lipaemia retinalis has varied considerably. Culler and Parker [4] reported that this condition will appear when the blood lipid rises above 3.5 Gm. per hundred cubic centimeters and disappear when it falls below 2.25 Gm., but marked individual variation has been the experience of other investigators.

The funduscopic appearance of lipaemia retinalis is both typical and striking. The retinal vessels assume a flat ribbon-like appearance of a pale cream to faint salmon shade in contrast to the normal pink to light maroon. Their caliber is greater than normal, and the arterioles are differentiated from the veins with difficulty. The arteriolar reflex is diminished or absent. Light ivory perivascular infiltration is frequently observed. If the choroidal circulation is not markedly involved, the disk and the fundus retain their normal color; otherwise the entire fundus assumes the strange ivory hue. Shortly after institution of insulin therapy the vessels in and about the optic disk manifest their normal appearance. The

Walter R. Parker Scholar for 1943, University of Michigan.

1. Heyl, A. G.: Tr. Am. Ophth. Soc. **3**:54, 1880.
2. Wagener, H. P.: Am. J. Ophth. **5**:521-525 (July) 1922.
3. Igersheimer, J.: Ocular Disturbances in Case of Acromegaly Complicated by Diabetes, Arch. Ophth. **27**:330-341 (Feb.) 1942.
4. Parker, W. R., and Culler, A. M.: Am. J. Ophth. **13**:573-584 (July) 1930.

abnormal features of the retinal vessels are maintained until the total plasma lipids drop to or below 2.25 Gm. per hundred cubic centimeters. The pathologic color and appearance of the retinal vessels are seen to originate in the remote periphery, gradually advancing toward the optic disk. Other than an occasional retinal hemorrhage, no abnormal funduscopic changes have been observed.

Patients with lipaemia retinalis are seriously ill and usually succumb to intercurrent infection more readily than the usual diabetic patient. The prognosis for life, however, is as good as in any case of diabetic coma. Insulin therapy has assured a moderately energetic state of well-being.

REPORT OF CASE

M. H., a white man aged 64, unmarried, a retired tailor, was admitted to the internal medicine service of the University Hospital Nov. 30, 1940. He appeared chronically ill. The chief complaint was "weakness and numbness of the legs," which had rendered him an invalid for six to eight months.

History.—Two years before admission the patient experienced sudden, terrific pain which extended the complete length of both legs. This pain persisted for one week and was followed by intermittent aching and acute discomfort. Six months prior to admission a local physician discovered that the patient had glycosuria. A measured diet and insulin therapy were advised, but the patient refused to use insulin. He had no appetite, and his diet was grossly inadequate. He lost 60 pounds (27 Kg.) in two years. Three months prior to admission there was a sudden loss of visual acuity in both eyes. The vision continued poor for ten days and then gradually returned to near normal.

The earlier history was noncontributory except to reveal persistent "indigestion" characterized by a sense of epigastric fulness after meals and much flatus.

Physical Examination.—The temperature was 97 F., the pulse rate 100, the respiratory rate 18, the blood pressure 110 systolic and 60 diastolic, the weight 92⅔ pounds (42 Kg.), and the height 66 inches (168 cm.). The patient was fairly well developed but severely emaciated and appeared chronically ill. The skin was dry. The ears, nose and throat were essentially normal. The mouth was edentulous. The lungs revealed slight dulness to percussion at the right axilla. The peripheral vessels were sclerotic. The heart was essentially normal. There were minor enlargement of the spleen and an inguinal hernia on the right. There was general atrophy of the musculature, particularly of the lower extremities. Neurologic examination disclosed peripheral paresis of the right seventh nerve, absence of the vibratory sense on the left and weakness of all the peripheral musculature.

The laboratory data are summarized in the accompanying table.

Course.—During the first week of hospitalization the patient's general condition and appetite improved as the diabetes mellitus rapidly came under fair control. Occasional elevations of the temperature to 100 F. were observed. A daily average of 40 Gm. of sputum was raised. On December 5 roentgenograms of the chest revealed dense consolidation of the base of the right lung at the level of the ninth and eleventh ribs posteriorly. The roentgenologist received an impression of bronchiectasis of the middle lobe of the right lung or suppurative pneumonitis. The patient had a grossly bloody stool on the morning of December 8. The hemoglobin content dropped to 35 per cent. The patient's condition rapidly declined despite emergency transfusions and intravenous administration of fluids, until his respirations ceased at 4:15 a. m. December 8.

Permission was granted for postmortem examination of the body but not of the eyes.

Ophthalmologic Findings and Follow-Up Examinations.—The patient had observed "floating specks" before both eyes for approximately three months prior to admission. Sudden diminution in visual acuity in both eyes, more marked in the right, had occurred at approximately the same time. Improvement in visual acuity was slow and had been interrupted by periods of remission. No ophthalmologist had been consulted.

On December 1 the uncorrected visual acuity was 6/30 in the right eye and 6/12 in the left. The pupils were uneven, the right measuring 3 mm. and the left 4 mm. The pupillary reflexes were sluggish but equal in the two eyes. The tension as measured with the new Schiøtz tonometer was 15 mm. of mercury in each eye. The eyes were straight in the primary position. The extraocular movements were normal. There was no regurgitation from the sacs. The point of basal convergence was 155 mm. There was inability to close the right lids associated with loss of function of the orbicularis oculi muscle. A minor loss of corneal sensation was

demonstrated on the right. The right palpebral fissure remained 5 mm. wide on attempted forceful closure. The cilia of the left lower lid contacted the corneal surface, which exhibited extensive scarring of the lower one third. Fresh linear corneal staining areas were demonstrated with 2 per cent fluorescein. Slit lamp examination revealed no pathologic changes in the anterior chambers. A rather extensive arcus senilis was present in each eye. The pupils dilated poorly, but no posterior synechiae could be seen.

Funduscopic examination of the right eye December 1 showed the lens and central media to be clear. The optic disk was oval vertically. The margins were distinct. A large physiologic depression with a vivid lamina cribrosa sclerae was present. There was no loss of nerve substance. The disk was paler than normal. The retinal vessels exhibited a most unusual light cream color, and differentiation of the arterioles and veins was most difficult. The caliber of the vessels appeared greater than normal, and they had a somewhat ribbon-like form. No macular or peripheral lesions were noted in the retina. The choroidal vessels were similar in color to the retinal vessels, resembling those of extensive choroidal arteriosclerosis.

The funduscopic appearance of the left eye resembled that of the right eye in almost all important details.

Summary of Laboratory Data

Blood	11/30/40	**Hemoglobin**	14.5 Gm. (Sahli)
		Red cells	4,900,000
		White cells	10,000
		Differential count normal	
	12/ 6/40	**Hemoglobin**	6.7 Gm. (Sahli)
		Red cells	2,000,000
		White cells	12,600
Plasma lipids *	12/ 1/40	**Total plasma lipid**	6.2 Gm. per 100 Cc.
		Cholesterol	875 mg. per 100 Cc.
	12/ 5/40	**Total plasma lipid**	2.5 Gm. per 100 Cc.
		Cholesterol	553 mg. per 100 Cc.
Stool	12/ 2/40	+ guaiac reaction	
	12/ 3/40	++ guaiac reaction; ++++ benzidine reaction	
Nonprotein nitrogen	12/ 3/40	28 mg. per 100 cc.	
	12/ 7/40	50 mg. per 100 cc.	
Urea clearance	12/ 3/40	1st specimen, 69% clearance	
		2d specimen, 53% clearance	

Urine	11/30/40	Reaction for Dextrose	Reaction for Acetone
	4 p. m.	++++	++++
	6 p. m.	++++	++++
	7 p. m.	++++	++++
	8 p. m.	++++	++
	9 p. m.	++++	++
	10 p. m.	++	0
	12/1/40, 10 p. m.-7 a. m.	0	0
	12/1/40-12/5/40	0 to ++++	None

* Henry Eckstein's method of determination of plasma lipids was used.

The diagnoses were lipaemia retinalis, both eyes; lagophthalmos, right eye; trichiasis, left eye, and spastic entropion, left eye.

The patient was carefully followed from day to day. No funduscopic changes were observed until December 5, at which time the major vessels in and about the optic disk showed a partial return to normal color. This gradually expanded toward the retinal periphery. The total fat content of the blood was 2.52 Gm. per hundred cubic centimeters on December 5. I had no opportunity to see the fundi after the intraintestinal exsanguination.

Pathologic Diagnoses.—Postmortem examination revealed gross or microscopic changes permitting the following diagnoses: chronic peptic ulcer of the pylorus with massive intestinal hemorrhage; exsanguination; diabetes mellitus; xanthomatosis diabeticorum (infiltrations of xanthoma cells in the spleen, bone marrow and glomeruli, with perineural and intraneural histocytes); diabetic neuritis; unresolved croupous pneumonia in the middle and lower lobes of the right lung, with cornification, multiple abscesses and early pulmonary gangrene; subacute fibrinous pleuritis; emaciation; serous atrophy of all adipose tissue; aortic and coronary atherosclerosis; multiple anemic infarcts of the myocardium; minimal subacute mitral thromboendocarditis; chronic passive congestion of the liver; small septic infarct of the kidney, and slight bilateral hydrocele.

COMMENT

This case is of interest for several reasons. Only 1 other case in which the patient was over 60 has been reported. The combination of severe emaciation, starvation, pneumonia, diabetes mellitus, infarct of the kidney, pulmonary abscesses and xanthomatosis is worthy of attention in that each alone can effect an elevation of the plasma lipid. It was probably because of this multiplicity of pathologic changes capable of influencing the concentration of lipid, associated with a state of acidosis, that lipaemia retinalis was produced in such a comparatively elderly patient. Since the disease is usually present only in young patients with severe diabetes, associated severe systemic complications are probably requisite to its manifestation in older patients, with milder diabetes.

Death in this case resulted from the intraintestinal exsanguination.

The diabetes was being fairly easily controlled despite the extensive severe pulmonary disease. Acidosis was absent within six hours after institution of dietary and insulin therapy.

The presence of xanthoma diabeticorum is interesting. It is possible that similar lipid histiocytes had invaded the optic nerve, which could account for the interference with visual acuity noted in the history. Visual fields were taken with the patient in bed, and no satisfactory data as to the status of the central fields could be obtained, although the peripheral fields were normal. Since no optic nerve tissue was studied, a diagnosis of optic (retrobulbar) neuritis is purely conjectural. The changes in refraction commonly experienced in diabetes must also be kept in mind as a course of the loss of visual acuity. I did not have an opportunity to perform a refraction.

The total blood lipid dropped to 2.52 Gm. per hundred cubic centimeters and there was not complete recovery of a normal retinal appearance. Culler and Parker found that lipaemia retinalis disappeared when the total blood fat fell below 2 Gm. per hundred cubic centimeters. McKee and Rabinowitch noted some evidence of lipaemia retinalis when the blood fat level was 1.65 per cent. The latter authors suggested individual variations as an explanation and also postulated the theory that anatomic changes in the vessel walls effecting an alteration in permeability is responsible. Marked damage to the vessels could easily have resulted in the present case as a sequela of the numerous severe systemic complications.

SUMMARY

The sixty-second case of lipaemia retinalis is reported.

The patient, aged 64, is the second oldest reported on to date.

The patient presented a most unusual combination of severe systemic diseases, complicating diabetes mellitus, all of which were capable of effecting hyperlipemia.

The level of blood lipid fell from 6.2 to 2.52 Gm. per hundred cubic centimeters before death.

Xanthoma diabeticorum was unusually widespread.

It is suggested that for lipaemia retinalis to be manifested in an elderly patient with mild diabetes, severe systemic complications such as the ones present in this case are requisite.

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RICKETTSIAS IN OPHTHALMOLOGY

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Little experimental work has been done on the rickettsias as related to ophthalmology. The inability to find any all-inclusive article on the subject prompted this paper, which is essentially a review of the literature. This topic is more important now, since the armed forces are engaged in combat in areas where rickettsial diseases are more frequent than in the United States.

MORPHOLOGY

Rickettsias are small, gram-negative, bacteria-like organisms, often pleomorphic, generally less than 0.5 micron in diameter, staining lightly with aniline dyes but well with Giemsa's stain, living and multiplying in arthropod tissues and acting as obligate intracellular parasites. Pinkerton [1] stated that forty-two micro-organisms described as rickettsias, all of which are nonpathogenic for mammals, have been observed in thirty-seven species of arthropods. Only four pathogenic organisms at present can be classified with rickettsias on the basis of the definition given: 1. Rickettsia prowazeki is named in honor of the two pioneers in the experimental study of rickettsia who died attempting to isolate the organism, Ricketts and von Prowazek. This is the cause of typhus fever, a louse-borne and flea-borne disease found endemically in many countries of Europe, where war, famine and unsanitary conditions exist. In North America, Mexico is the main site of typhus. Many American soldiers surviving this disease may return home with ocular complications; therefore it behooves ophthalmologists to be informed about all the rickettsial diseases. 2. Rickettsia dermacentroxenus is the cause of tick-borne Rocky Mountain spotted fever, endemic in the Rocky Mountain area. 3. Rickettsia tsutsugamushi (or Rickettsia orientalis) is the exciting agent of tsutsugamushi fever, a mite-borne disease endemic in Japan. Nagayo, as will be shown later, experimentally produced this disease in rabbits by injection of rickettsial organisms into the anterior chambers. 4. Rickettsia ruminantium is the cause of tick-borne heartwater in sheep, goats and cattle.

The general classification of rickettsias is ill defined. Pinkerton, in attempting to clarify this, suggested the bacterial family name of Rickettsiaceae for the pathogenic rickettsias. As a typical representative of this group, R. prowazeki merits a description. This organism has an average size of 300 millimicrons but may be smaller. It is ordinarily nonfiltrable through a Berkefeld filter and appears intracellularly as a pleomorphic organism. Most characteristically it is a minute diplobacillus averaging 0.6 by 0.3 micron. Occasionally short chains are seen. It stains poorly with aniline dyes and is gram-negative but cannot be recognized with certainty by means of the Gram stain. The Giemsa stain reveals the organisms as

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1. Pinkerton, H.: The Pathogenic Rickettsiae, Bact. Rev. **6**:37-78, 1942.

blue or purple bodies, with the cytoplasm a pale blue. Typical organisms need living cells for their growth. They multiply rapidly in various mediums containing living cells used for ordinary virus cultivation, for example plasma tissue culture.

Rickettsias are obligate intracellular parasites, like the viruses, but are more facultative than the latter in that they have a more complex enzyme system, which allows a certain amount of independent metabolic activity within the host cells. They can be seen clearly in unstained living cells with dark or light illumination, and their movement can be watched. R. prowazeki, the organism of typhus, multiplies only in the cytoplasm in tissue cultures, and not in the nuclei, whereas R. dermacentroxenus, the organism of Rocky Mountain spotted fever, grows in the nuclei. R prowazeki is readily killed by heating, drying or use of chemical agents.

A diagnostic means for diagnosis of the rickettsial diseases is the Weil-Felix reaction, which depends on the principle that certain strains of Proteus vulgaris, especially OXK and OX19, are agglutinated by the serum of patients infected with typhus or spotted fever. R. prowazeki agglutinates generally with a high titer of the OX19 and a low titer of the OXK strain. The reverse is true for R. tsutsugamushi. Infections with rickettsial diseases usually confer long-lasting immunity.

Except for minor variations, the other pathogenic rickettsias are similar to the typhus organism in their morphologic, cultural and staining reactions.

Rickettsias have many features in common with certain bacteria and also with some viruses. Their visibility, morphologic characteristics and nonfiltrability closely ally them with the bacteria. Their staining reaction (with Giemsa's stain), growth requirements (tissue cultures) and specificity for certain cell types are points of similarity with the viruses. The most logical view, proposed by Pinkerton, is that rickettsias are bacteria which have become adapted to intracellular life in arthropod tissues. They occupy an intermediate position between viruses and bacteria. It is not wise to draw definite boundaries between the three groups, but it is of paramount importance to remember that rickettsias are different from viruses and bacteria (fig. 1).

RICKETTSIAS IN OPHTHALMOLOGY

The preceding discussion has been limited to rickettsias in general. Attention is now directed to the study of rickettsias in ophthalmology. This will include laboratory experiments on animals, especially rabbits; clinical observations on human beings, and, finally, investigation of ocular lesions caused by the various pathogenic rickettsias.

Coles [2] studied acute and subacute conjunctivitis of sheep, oxen, goats, fowls and domestic pigs. Conjunctival scrapings from the infected eyes were examined microscopically with the Giemsa stain. Rickettsia-like organisms were described by Coles, who named each organism differently according to the host. Although this author stated the belief that the exciting agent was a rickettsia, its similarity to inclusion bodies, especially the elementary forms, leaves one in doubt as to its exact nature. Furthermore, an arthropod host was absent in all the instances of animal conjunctivitis.

Johnson [3] reported 200 instances of pannus formation in sheep, stating the belief that the etiologic agent was of rickettsial nature. This pannus formation (inter-

2. Coles, J. D. W. A.: Rickettsial-Like Organisms of Conjunctival Epithelium (Inclusions) of Pig, Arch. Ophth. **25**:101-112 (Jan.) 1941.

3. Johnson, L. V.: A Pannus-Forming Infection in Sheep's Eyes, Proc. Soc. Exper. Biol. & Med. **38**:42-43, 1938.

stitial) closely simulated that found in trachoma. The intensity of his scientific investigation is reflected by the fact that every sheep had a slit lamp examination. Undoubtedly, as will be brought out later, in the discussion of trachoma, the recognition of rickettsias is essentially a question of interpretation.

One of the most conclusive and exhaustive experimental studies to determine the exciting cause of tsutsugamushi fever was performed by Nagayo and his co-workers.[4] They obtained rickettsial organisms from different sources, such as emulsions of macerated testicles, lungs and lymph nodes of rabbits, guinea pigs and monkeys. All of these animals had a disease which closely simulated human tsutsugamushi fever. Nagayo injected the infected material into the anterior chambers of the right eyes of 500 albino rabbits, using the left eyes as controls. After an incubation period varying from four to eight days, ocular lesions developed in the following order: (1) hyperemia of the iris with circumcorneal injection, (2)

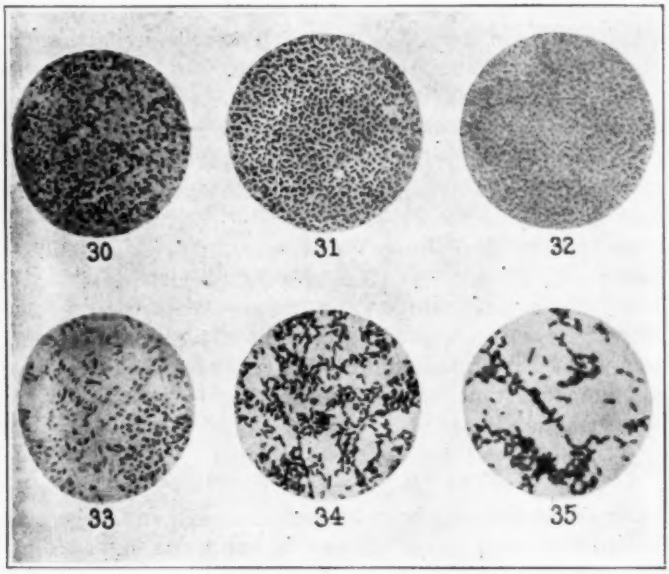

Fig. 1.—Rickettsias observed in Rocky Mountain spotted fever. (From Noguchi, H.: J. Exper. Med. **43**:515, 1926.)

typical serous iritis, (3) clouding of the posterior surface of the cornea, (4) early pannus formation at the limbus and (5) formation of keratitic precipitates and extension of the pannus to the center of the cornea.

After approximately one month there was a marked retrogression of symptoms. There was beginning clearing of the cornea, especially near the limbus, and the iritis subsided. Complete resolution occurred in forty days, with a residual scar in the cornea.

Nagayo found that the infected eye acquired a complete immunity against another inoculation, but the other eye of the same animal did not have such immunity.

4. Nagayo, M., and others: (*a*) Ueber den Nachweiss des Erregers der Tsutsugamukrankeit Rickettsia, Jap. J. Exper. Med. **9**:87-150, 1931; (*b*) On the Virus of the Malady of Tsutsugamushi Fever, Compt. rend. Soc. de biol. **104**:637-641, 1930.

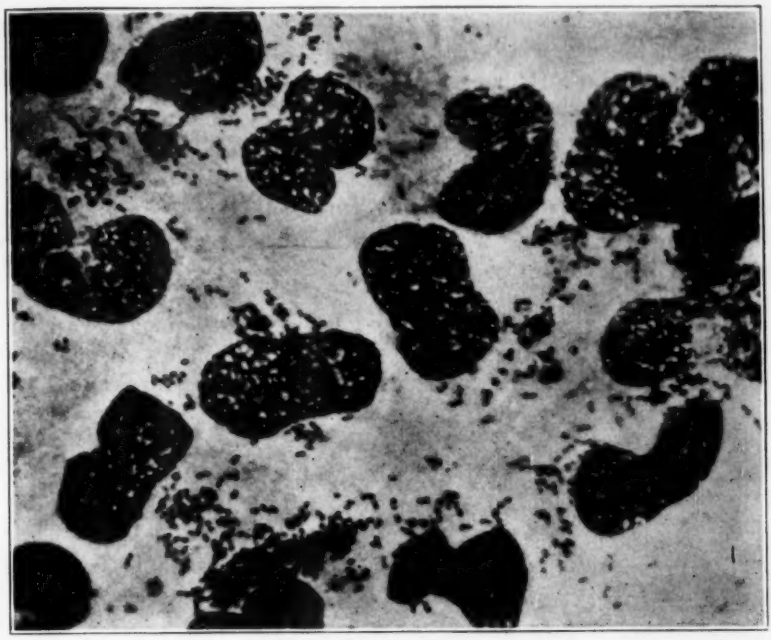

Fig. 2.—Streak preparation showing the endothelial cells of the cornea, with marked invasion of rickettsial organisms, in tsutsugamushi fever. (From Nagayo.[48])

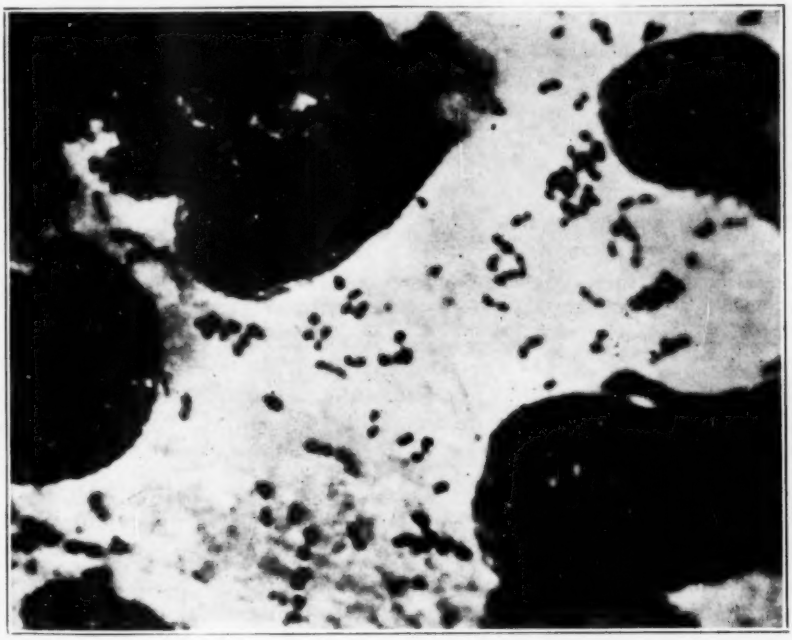

Fig. 3.—The preparation shown in figure 2 under higher magnification (× 2.5). (From Nagayo.[48])

Microscopic examination revealed lesions like those seen in human tsutsugamushi fever. There was an abundant infiltration of rickettsial bodies in the endothelial cells of the cornea. The rickettsial organisms were found in the inflamed tissues of the iris and ciliary body in the interior of infiltrated histiocytes. The aqueous humor failed to show these bodies.

Nagayo came to the following conclusions:

1. The organisms seen with the Giemsa stain are different from preexisting protoplasmic granules or pathologic nuclear products.

2. The organisms are always present in experimental animals infected with rickettsial material but not in control animals.

3. The number of organisms present in an ocular lesion is proportional to the intensity of the lesion and to the pathogenicity of the aqueous humor.

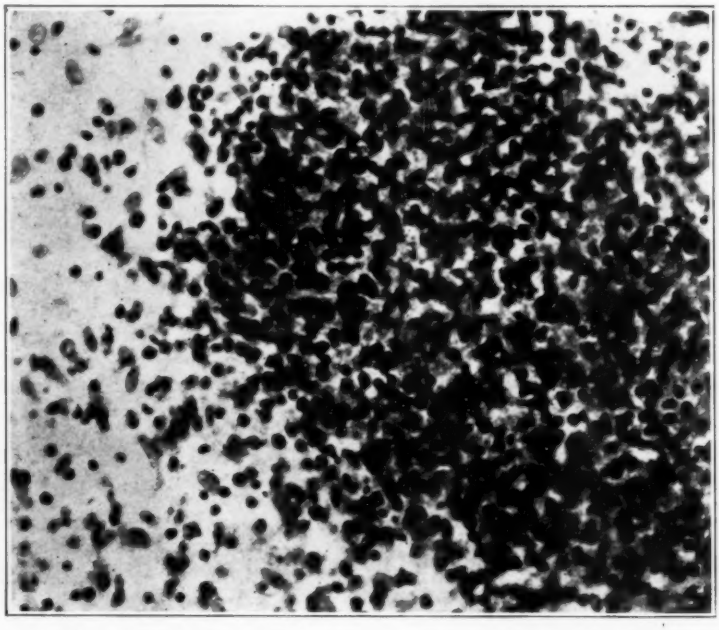

Fig. 4.—Beginning regressive changes in a nodule of the iris (tsutsugamushi fever) necrosis in the center and karyorrhexis and pyknosis of the mononuclear cells and lymphocytes. (From Nagayo.[4a])

4. The ocular lesions of monkeys and guinea pigs produced with the same material were similar to those in rabbits, with especial emphasis on the discovery of rickettsial bodies in the endothelial cells of Descemet's membrane.

5. One attack seems to confer lasting immunity.

6. The offending rickettsial organisms are found in various tissues of human beings and monkeys afflicted with this disease.

Nagayo called the organism responsible for this disease in rabbits R. orientalis. It was on the basis of the form, staining reaction, nonmotility, nonfiltrability, intracellular localization, difficulty of cultivation and mode of infection (by the bite of a mite) that he concluded that the responsible organism was a rickettsia (figs. 2, 3 and 4).

TRACHOMA

The literature is replete with reports on experimental work on the etiology of trachoma. Probably there is no ophthalmologic disease concerning which more discussion exists as to the true nature of the exciting agent. Hence the causation is still uncertain. There are two distinct schools of thought: One maintains that the cause is a rickettsia, and the other insists on a virus as the etiologic agent. Evidence for both theories will be presented.

Cuénod and Nataf [5] are the chief proponents of the rickettsial nature of trachoma. They found that there was a definite correlation in geographic distribution between trachoma, lice and human rickettsial disease. They were successful in obtaining rickettsial bodies from the intestines of lice experimentally infected intra-anally with trachomatous material. Cuénod described what he called rickettsial elements of the two types on follicles in trachoma: One was small and analogous to elementary bodies and the other larger and analogous to initial bodies.

These workers obtained a human volunteer with one eye blind as a result of injury. The conjunctiva and cornea were normal biomicroscopically and bacteriologically. The procedure and results of their experiment were as follows: An emulsion of crushed lice infected with trachomatous material was injected subconjunctivally. After an incubation period of eight days there appeared a crop of follicles along the tarsal and supratarsal portion of the conjunctiva. Tears and ocular secretions contained epithelial cells loaded with inclusion bodies. Later rickettsial bodies were seen scattered throughout the protoplasm of the epithelial cells. Sixty days after the onset of symptoms the patient presented all the clinical signs of trachoma.

Cuénod and Nataf concluded that infection in trachoma occurs in two ways: directly from person to person through contamination with tears which contain rickettsias and indirectly from bites by body or head lice carrying rickettsias.

Busacca [6] reported certain bodies in the follicles and epithelial cells of trachomatous patients. With the Giemsa stain, many of these look like elementary bodies in the epithelial cells, but he called them rickettsias.

Poleff [7] inoculated the anterior chambers of rabbits, guinea pigs and chickens with trachomatous material and obtained an intraocular and conjunctival folliculosis, followed by a cicatrization of the follicles. He found small discrete coccoid bodies (like elementary forms) and called them rickettsia-like elements. He grew these organisms in tissue culture and concluded that the human cornea is the best medium for the growth of rickettsias.

Apparently the proponents of the rickettsial theory of trachoma brought investigators into the field who disagreed with their findings. Prominent among these were Thygeson [8] and Julianelle.[9] The former examined trachomatous material in stained specimens sent from Tunis by Cuénod and Nataf, slides sent from Brazil

5. Cuénod, A., and Nataf, A.: Bacteriological and Experimental Researches on the Etiology of Trachoma, Brit. J. Ophth. **21**:309-315, 1937.

6. Busacca, A.: Is Trachoma a Rickettsial Disease? Arch. Ophth. **17**:117-126 (Jan.) 1937.

7. Poleff, L.: Passage des "corpuscles rickettsoïdes" du trachome sur le tissu de l'oeil humain hors de l'organisme et quelques observations générales sur la culture des dites formations in vitro, Rev. internat. du trachome **16**:79-87, 1939; abstracted, Brit. J. Ophth. **23**:641, 1939; Culture in Vitro of Corpuscles of Trachoma, ibid. **23**:738-740, 1939; abstracted, Arch. Ophth. **25**:169 (Jan.) 1941.

8. Thygeson, P.: Problem of Rickettsia in Trachoma, Arch. Ophth. **20**:16-18 (July) 1938.

9. Julianelle, L. A.: Studies on the Pathogeny of Trachoma, Brit. J. Ophth. **22**:336, 1938. Julianelle, L. A., and Smith, L. E.: Studies on the Infectivity of Trachoma: Immunological Aspects of Rickettsial Concepts, Am. J. Ophth. **23**:62-67, 1940.

by Busacca and, finally, material from the United States, all for rickettsial organisms. Only the elementary and initial bodies of the epithelial cell inclusions of trachoma were observed, and no true rickettsias. Thygeson therefore stated the belief that trachoma is due to a virus which passes only filters with large pores. The formations that other workers reported in large numbers in trachomatous follicles, he said, were probably cell granules and cytoplasmic debris.

Thygeson,[8] like Cuénod and Nataf, was successful in obtaining a human volunteer. He injected trachomatous material which had been filtered through Elford membranes, of such pore size that elementary bodies went through, into the eye of the subject. Typical trachoma with inclusion bodies developed, confirming Thygeson's view that trachoma is a virus disease.

According to Julianelle,[9] who studied the agglutination reaction of serums from trachomatous and nontrachomatous patients with OX19 and OX2 strains of P. vulgaris, the Weil-Felix reaction has no use as a diagnostic sign for trachoma. He thus does not agree with the earlier workers mentioned in Bengtson's article.[10]

Braley [11] concluded from study of smears prepared with Giemsa's stain that the bodies observed by Cuénod and Nataf were stained mitochondria and keratin granules rather than rickettsias. He expressed the opinion that the offending organism is a virus. He [12] also studied a family of Fort Apache Indians infested with lice and diseased with trachoma. Less than 1 per cent of the lice had rickettsias in their intestinal tracts. Ground lice from the Indians did not transmit conjunctival disease to baboons, nor did such lice infested with trachomatous material. Braley therefore concluded that the louse is not a vector in trachoma.

De Rötth [13] was unsuccessful in repeating the experiments of Cuénod and Nataf, i. e., infecting monkeys with lice which had been infected with trachomatous material by the anal route. The appearance of follicles does not prove the transmission of trachoma. He agreed with Thygeson that rickettsias are not the causative agent in trachoma.

The most comprehensive article on the question of rickettsias in trachoma was written by Ida R. Bengtson.[10] She reviewed the literature and studied the Weil-Felix reaction, using OX19, OX2 and OXK proteus strains. A comparison of results obtained with trachomatous and normal serums shows no significant differences. Also, agglutination tests with trachomatous serums and suspensions of rickettsial organisms (from subjects with typhus and other fevers) were performed. No agglutination with any of the antigens and therefore no evidence of an antigenic relationship was noted. According to Bengtson the theory of rickettsias in trachoma involves a question of the nature of these organisms. The criteria mentioned previously in this paper, that rickettsias are small bacillary bodies, obligate intracellular parasites with an arthropod host, which stain well with Giemsa's stain and grow poorly on artificial culture mediums, are not satisfied in the case of trachoma. The louse has not been proved to be the transmitting vector. The Weil-Felix reaction has no diagnostic value. Bengtson further stated that the offending organism in trachoma is not rickettsia because the morphologic appearance of the bodies seen in this disease look like definite inclusion bodies (elongated or rod-shaped initial bodies and small coccoid elementary bodies, both

10. Bengtson, I. R.: Question of Rickettsial Nature of Trachoma, Am. J. Ophth. **23**:770-779, 1940.

11. Braley, A. E.: Rickettsial Question in Trachoma: Microscopic Observation on the Virus, Arch. Ophth. **21**:735-740 (May) 1939.

12. Braley, A. E.: Rickettsial Question in Trachoma: Louse as a Possible Disseminating Agent for the Virus, Arch. Ophth. **22**:262-270 (Aug.) 1939.

13. de Rötth, A.: Problem of Etiology of Trachoma, Arch. Ophth. **22**:533-539 (Oct.) 1939.

in the cytoplasm of the epithelial cells). Their appearance differs considerably morphologically from the bacillary types of rickettsias seen in typhus and Rocky Mountain spotted fever.

Bengtson therefore concurred with Thygeson and Julianelle in believing that trachoma is caused by a filtrable virus and not a rickettsia. As proof she cited the following evidence: the morphologic nature of trachoma organisms, which are inclusion bodies, the elementary forms being filtrable; their growth characteristics in cells; their more complicated life cycle; the presence of a matrix; the differential staining with Giemsa's stain; the negative Weil-Felix reaction, and the lack of proof that the louse is the arthropod host.

It is indeed hard to explain the variation in results. Possibly there are several types of trachoma, each a separate entity with its own exciting agent. Otherwise it is extremely difficult to account for the dissension in the experimental conclusions. Perhaps the entire matter is one of interpretation and not of observation. Julianelle put it aptly when he stated, "Virus, rickettsiae, and inclusion bodies are not as divergent as they appear: differences are less of fact and more of definition and classification."

RICKETTSIAS IN HUMAN DISEASES

Of the three known rickettsial diseases in human beings, Rocky Mountain spotted fever affects the eye least. Most of the patients have only a mild catarrhal conjunctivitis. According to Nagayo,[4] the changes in tsutsugamushi fever in human beings are essentially similar to those found by him in his experimental work with rabbits. To recapitulate, these are hyperemia of the iris, mild conjunctivitis, clouding of the cornea and anterior chamber, iridocyclitis with keratitic precipitates and pannus formation; there is gradual recession of the symptoms with clearing of the infection and residual scar formation in one to two months.

In typhus fever, according to Dantrelle,[13a] the following ocular changes are observed: The milder symptoms are hyperemia of the conjunctiva, subconjunctival ecchymosis, ciliary alopecia, miosis, photophobia, hyperemia of the fundus, mydriasis during convalescence and night blindness. Photophobia is so severe at times that the patient is unable to observe ordinary daylight and seeks relief by hiding his head under the pillow. Miosis invariably means a poor prognosis.

The more severe symptoms in typhus can be divided into two groups: those of the febrile stage and those of convalescence. The former consist primarily of: (1) discoloration of the iris associated with secondary cataract, which can develop in one to two months; (2) perivascular changes in the fundus with pigmentation along the retinal vessels; (3) optic neuritis leading to atrophy of the optic nerve and complete blindness, and (4) ocular palsies of the third and sixth nerves. The complications of convalescence are: (1) palpebral abscesses, which usually show streptococci as the secondary invaders; (2) orbital phlegmon appearing on the seventh to tenth day of convalescence and leading usually to exophthalmos in which the eye is turned down and out, the abscess being in the upper and inner portion of the orbit; (3) corneal ulcers, which appear in the first week of convalescence and usually involve the lower portion of the cornea, with perforation and blindness as not infrequent complications, and (4) atrophy of the optic nerve.

There is no specific treatment for the rickettsial ophthalmic diseases. General constitutional measures and local symptomatic therapy are indicated. The local ocular disorder is treated according to general ophthalmologic principles. Elliott [14]

13a. Dantrelle, A., cited by Elliot.[14]

14. Elliot, R. H.: Tropical Ophthalmology, London, H. Frowde, 1920, pp. 492-496.

stated the belief that most of the treatment should be centered around prophylactic measures. He advocated early incision and drainage of all abscesses. In cases of optic neuritis he advised the use of strychnine and daily galvanization.

A recent news item from Berne, Switzerland, reported an epidemic of typhus fever in the European countries at war, especially Germany, Poland and Russia, and in North Africa. Since many American soldiers are now, or may be in the future, stationed in these countries, it is unnecessary to emphasize again that a knowledge of the rickettsias in ophthalmology is important.

SUMMARY AND CONCLUSIONS

A comprehensive review of the literature supports the fact that the rickettsias are different from viruses and bacteria.

Coles stated the belief that rickettsias may cause conjunctivitis in various animals. Johnson has shown that pannus formation in sheep can be caused by rickettsial organisms.

Nagayo has experimentally produced the ocular lesions of tsutsugamushi fever in rabbits with injections of rickettsial organisms into the anteror chamber.

The arguments of adherents to the rickettsial and to the virus etiologic viewpoint on trachoma have been presented.

Of the known human rickettsial diseases, typhus fever causes the most characteristic ocular changes.

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BLOOD CHOLINESTERASE VALUES OF PATIENTS WITH GLAUCOMA

ANDREW RADOS, M.D.
NEWARK, N. J.

Studies of cholinesterase were begun about seventeen years ago by Loewi [1] and his co-workers. These authors proved that the effects of stimulation of the vegetative nervous system are transmitted to the effector organs through humoral channels. Loewi demonstrated that stimulation of the cardiac branch of the vagus nerve gives rise to a vagotropic substance, which likewise is liberated by stimulation within the sympathetic and parasympathetic nervous systems. The liberated substance in all probability represents acetylcholine. Loewi and Navratil observed that aqueous extract of frog heart destroyed the so-called vagus substance, which was found to be indistinguishable from acetylcholine. The destructive agent was thermolabile and possessed other characteristics of an enzyme, and hence it was considered an acetylcholine esterase. Engelhart showed on isolated frog heart that physiologic excitation of the oculomotor nerve causes acetylcholine to appear in the aqueous. Dale would call the substances cholinergic, disregarding the anatomic origin in the sympathetic or parasympathetic nervous system; the oculomotor nerve, the cardiac branch of the vagus nerve, the secretory nerves, the nerves of the sweat glands and some of the paraganglionic sympathetic nerves belong to this group. On the other hand, the vegetative nerves, which on stimulation liberate epinephrine or epinephrine-like substances, form the adrenergic group; here belong the accelerator fibers of the heart and the sympathetic fibers of the dilator of the pupil.

Acetylcholine is rapidly inactivated through hydrolytic splitting into choline and acetic acid through the esterase. The enzyme is present in the blood and in various organs and tissues. The specific or polyvalent nature of the ferment is questionable. The enzymatic breakdown of the accumulated acetylcholine regulates the time and intensity of the cholinergic reaction produced by the stimulation of nerves.

In a second paper Loewi and Navratil [2] proved that physostigmine, which potentiates the action of the vagus nerve, inhibits the enzymatic decomposition of the so-called vagus substance and acetylcholine. Engelhart and Loewi [3] demonstrated the enzyme nature of this agent. Stedman, Stedman and Easson [4] showed that the enzyme in question differs from other known esterases and proposed that it be called cholinesterase. The same authors studied its nature and properties extensively and found that it can be purified by salting-out procedures and adsorption on aluminum oxide or ferric hydroxide. The enzyme appeared to be associated with the protein fraction, soluble in 35 per cent ammonium sulfate solution but precipitated at 40 per cent salt concentration in a slightly acid medium.

The discovery of acetylcholine suggested the possibility that it assists in the regulation of the intraocular pressure. According to Passow [5] the instillation of acetyl-

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1. Loewi, O., and Navratil, E.: Arch. f. d. ges. Physiol. **214**:678, 1926.
2. Loewi, O., and Navratil, E.: Arch. f. d. ges. Physiol. **214**:689, 1926.
3. Engelhart, E., and Loewi, O.: Arch. f. exper. Path. u. Pharmakol. **150**:1, 1930.
4. Stedman, E.; Stedman, E., and Easson, L. H.: Biochem. J. **26**:2056, 1932.
5. Passow, A.: Arch. f. Augenh. **103**:111, 1936.

choline in glaucomatous eyes causes a distinct, even if transient, tension-depressing effect. The short duration was explained by the enzymatic decomposition of the substance during its diffusion into the ocular tissues. The tension-reducing property of physostigmine is due to accumulation of acetylcholine in consequence of the inhibition of esterase activity.

Velhagen [6] studied the occurrence of vagotropic substances in the aqueous, the retina and the choroid of cats (employing the older biologic method, the Fuehner method with leeches), and emphasized the presence of acetylcholine in the retina and choroid. Plattner and Hintner [7] worked with aqueous and iris extracts. The results of Uvnäs and Wolff [8] are in contradiction to those of the previous authors. They did not find acetylcholine esterase in the aqueous of bovines except when it appeared as a postmortem change or in the second aqueous after partial emptying of the anterior chamber, which is in accordance with the fact that the enzymatic action is linked to the protein molecule. Considerable quantities of the esterase were found in the vitreous, the activity corresponding to one eighth of the activity of the blood of man and of the horse. The vitreous of horses showed less esterase than did that of bovines. The contradiction to the results of Velhagen and of Plattner and Hintner is explained by technical factors, that is, the inflow of vitreous after the puncturing and too thorough emptying of the anterior chamber in their experiments. Recently Herrman and Friedenwald [9] reported moderate similar cholinesterase activity in the choroid plexus and the processes of the ciliary body. According to these authors there is no evidence that the secretory activity of either organ is cholinergic. The esterase activity of the stroma of these tissues is relatively high compared with that of the epithelium.

Turning from research on the presence of acetylcholine and its esterase in the tissues of the eye under physiologic conditions, one finds only scanty notes on its significance in pathologic conditions. According to Passow the blood of patients with glaucoma shows smaller amounts of choline and therefore larger amounts of the antagonistic epinephrine-like substances than normal. Independently of and previous to discussion of acetylcholine, there appeared clinical observations of various authors connecting glaucoma with the sympathicus, elimination of the latter (by excision of the superior cervical ganglion or use of ergotamine) resulting in a decrease of the intraocular pressure. Pletneva, Raeva and Voronina [10] made a biologic analysis of the aqueous of patients with glaucoma. They obtained the aqueous during operations for cataract and glaucoma; it was diluted with Ringer solution 1:10 or 1:20 and put through isolated frog heart, and the action was registered by kymograph. Fifty-five glaucomatous eyes, 41 cataractous eyes and 4 eyes with traumatic iridocyclitis were examined. In 52 per cent there was a sympathicotropic and in 34 per cent a vagotropic substance, i. e., a substance causing acetylcholine activity, or retardation of the heart action. Since such retardation may be caused by histamine as well as by acetylcholine, the authors examined defibrinated blood from 2 glaucomatous and 3 nonglaucomatous patients with increased acetylcholine in the aqueous; they found the heart rhythm unchanged in all.

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6. Velhagen, K.: Arch. f. Augenh. **103**:424, 1930; **104**:546, 1931; **105**:573, 1932; **109**:195, 1936.

7. Plattner, F., and Hintner, H.: Arch. f. d. ges. Physiol. **225**:19, 1930.

8. Uvnäs, B., and Wolff, H.: Occurrence of Acetylocholinesterase in the Aqueous Humor and Vitreous Body, Acta ophth. **16**:157, 1938.

9. Herrman, H., and Friedenwald, J. S.: The Choline Esterase Content of the Choroid Plexus and Ciliary Processes, Bull. Johns Hopkins Hosp. **70**:14, 1942.

10. Pletneva, P.; Raeva, N., and Voronina, E.: Vestnik oftal. **13**:462, 1938.

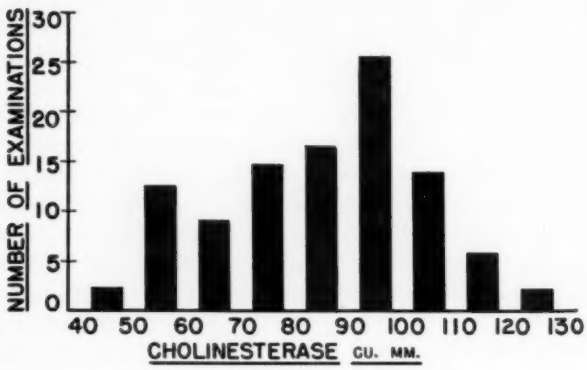
Until 1932 the rate of enzymatic destruction of acetylcholine could be determined only by biologic testing; this is less exact than the chemical method of Stedman,[11] in which assay of the acetylcholine-splitting enzyme in the blood is based on titration of the acid liberated by hydrolysis of acetylcholine at a constant p_H. A further improvement was made in 1933 by Ammon,[12] who employed a gasometric method, determining the amount of carbon dioxide liberated from a carbonate solution by the acid formed from the hydrolysis of the acetylcholine substrate. The carbon dioxide was measured in the Barcroft-Warburg respirometer, and the amount formed served as an index of the acetylcholine-splitting power. In the meantime, Stedman independently devised a method, utilizing the Barcroft differential apparatus, which was based on the same principle. The advantages of these methods in comparison with titration procedures are obvious, since red blood cells and colored solutions can be tested, whereas pigments interfered with the older procedures. In the investigations here reported a modified Ammon method was used, as described by Antopol, Tuchman and Schifrin.[13] At first these authors modified the Ammon method so that the reaction was continued over a two hour period at 30 C. They later doubled the volume of the serum and substrate solutions and used a one hour period in order to shorten the determinations and avoid the flattening of the activity time curves which sometimes occurred with the more active serums when a two hour interval was used. The activity was based on the slope of the linear portion of the curve. The values were expressed in cubic millimeters of carbon dioxide liberated from 7.5 mg. of acetylcholine chloride in 1.5 cc. of bicarbonate solution (Ringer's solution) by 0.5 cc. of serum diluted fifty times with bicarbonate solution (Ringer's solution).

In view of the observations which had been made on acetylcholine in the blood it was desired to make a study of the blood cholinesterase in patients with glaucoma. Until recently most investigators have considered acetylcholine per se and have almost disregarded the enzyme which destroys this substance. It should be repeated that it has been proved that transmission of stimulation of the vagus nerve is effected by means of a chemical substance. This substance behaves much like acetylcholine, both physiologically and chemically. The disadvantage in its study and use lies in the fact that it acts over a very short period because it is so rapidly destroyed in the body. The rapid hydrolysis is affected by the esterase, which splits it into acetic acid and choline. Neither of these end products can produce the profound effects of their mother substance.

The normal values for blood cholinesterase range according to Ammon between 60 and 100 cu. mm. and according to Antopol and his co-workers between 40 and 120 cu. mm.

The blood of 61 patients with glaucoma was examined and 103 determinations of the cholinesterase made. The blood of 24 patients was examined once, that of 29 patients twice, that of 5 patients three times and that of 1 patient four times. The accompanying table summarizes the results. Repeated examination of blood from the same patient disclosed only slight variations. In order to make the results more comprehensible a chart was constructed. This demonstrates that the blood of the largest number of patients showed values between 90 and 100 cu. mm., the curve approaching slowly the smaller and steeply the higher values. The lowest values (between 40 and 50 cu. mm.) and the highest values (between 120 and

11. Stedman, E.: J. Physiol. **84**:56, 1935.
12. Ammon, R.: Arch. f. d. ges. Physiol. **233**:486, 1933.
13. Antopol, W.; Tuchman, L., and Schifrin, A.: Proc. Soc. Exper. Biol. & Med. **36**:46, 1937. Schifrin, A.; Tuchman, L., and Antopol, W.: Am. J. Digest. Dis. **9**:342, 1942.



Graphic presentation of the blood cholinesterase values of 61 patients with glaucoma.

Blood Cholinesterase Values for 61 Patients with Glaucoma (103 Examinations)

Range of Values (Cu. Mm.)	Values at Individual Examinations	Total Number of Examinations	Number of Examinations with Acute Glaucoma
130-120	• •	2	2
120-110	• • • • • •	6	4
110-100	• • • • • • • • • • • • • •	14	3
100-90	• •	26	3
90-80	• • • • • • • • • • • • • • • • •	17	1
80-70	• • • • • • • • • • • • • • •	15	2
70-60	• • • • • • • • • •	9	1
60-50	• • • • • • • • • • • • • • •	12	0
50-40	• •	2	1
Total		103	17

130 cu. mm.) were each registered for only 2 patients. These investigations revealed that the blood cholinesterase content of patients with glaucoma is within the normal range. This fact is the more interesting because in certain conditions, such as untreated hyperthyroidism, the values are relatively high, while in jaundice, cirrhosis of the liver, hepatitis, anemia, arthritis, rheumatic fever and hyperpyrexia they are pronouncedly depressed.

It was interesting to note that the values for the 12 patients with acute glaucoma were relatively high. They were as follows (expressed in cu. mm.): patient 1, first examination 86 and second examination 91; second patient, first examination 74 and second examination 80; patient 3, 112; patient 4, 95; patient 5, 106; patient 6, first examination 125 and second examination 114; patient 7, first examination 112 and second examination 127; patient 8, 66; patient 9, first examination 93 and second examination 94; patient 10, 48; patient 11, 102, and patient 12, 108.

SUMMARY

Of 61 unselected patients with glaucoma, 59 had blood cholinesterase values between 40 and 120 cu. mm., that is, within the normal range. The majority had high normal values. Of the 12 patients with acute glaucoma, only 2 had comparatively low values; the remaining 10 had values which were toward the upper limit of normal. It must be borne in mind that the normal values present a fairly broad band, and caution must be exercised in interpretation, especially in view of the additional fact that many conditions are likely to influence the blood cholinesterase. Such conditions are hyperthyroidism, anemia, carcinomatosis, cachexia, sepsis, subacute bacterial endocarditis, pneumonia and ulcerative colitis. In evaluation of the blood cholinesterase levels of patients with glaucoma such conditions must be excluded.

31 Lincoln Park.

Clinical Notes

ALLERGIC CONJUNCTIVITIS FROM COLORED INK

MAJOR ROBERT B. LEWY, MEDICAL CORPS, ARMY OF THE UNITED STATES

Now that allergy has become an established part of diagnosis, it is an integral part of the questioning phase of the adequate medical history. Allergic phenomena caused by unusual agents range from intestinal distress to epiphora. Many have been reduced to the commonplace with modern cutaneous testing and medical histories. The known locations of reactions and types of irritating substances are many and varied, and only an occasional new allergen or focus of action is discovered. The following account records an unusual but real cause of distress:

Private R. D. was sent to the eye, ear, nose and throat clinic of a station hospital somewhere in Australia. The provisional diagnosis by his dispensary physician was acute recurrent bilateral conjunctivitis of undetermined cause.

The patient was well built and muscular, in good health but complaining of redness and burning of both eyes. The vision was normal. The reaction was limited to the eyes. Of these the left was the more intensely affected. The bulbar conjunctiva was severely injected, especially around the limbus. The cornea appeared normal. There was slight epiphora. There was slight injection of the palpebral conjunctiva. The right eye was similar in appearance but was considerably less red.

The history was of interest. The patient stated that he had had similar attacks for the past six or seven years and that one this year was so severe that the left eye was almost blind. The attacks seemed to occur at intervals of two weeks or a month.

The periodicity suggested that the complaint might be due to a hypersensitivity. Therefore the standard questions regarding allergy were asked. Was he sensitive to horse dander, to dogs, to cats or to flowers? Did he have hay fever? Did angora sweaters make him sneeze? All these questions received a negative answer. When asked, "Have you noticed any trouble when reading the comic section of the Sunday paper?" he answered that his eyes watered when he read colored print and that he had noticed this reaction for some time but had not thought much about it.

Because of this clue investigation was instituted on colored print. The first day he was given a colored ink comic section to read. The increase in the ocular injection and epiphora was noticeable. The next day he was recalled for cutaneous testing. Various preparations of the commoner comics and rotogravure sections were patched against his skin. Dry, wet and macerated preparations were used.

On the following day the patches were removed. There was no dermal reaction, and the provisional diagnosis appeared to be wrong. This concept was overruled by further thought, and further experimentation satisfactorily established the diagnosis. The subject was again exposed to colored print. The eyes watered and became injected. One drop of a suspension of the comic section in water was placed in the conjunctival sac. This caused a definite increase in the ocular injection. A small bit of colored paper was placed against the bulbar conjunctiva. Both eyes became intensely red. A drop of epinephrine hydrochloride instilled in each eye promptly relieved the congestion and the discomfort.

In retrospect, the failure of the skin to react to the patch test became a comforting part of the diagnostic evidence. As the patient had ocular sensitivity but did not show, either simultaneously or later, a dermatitis from the handling of the colored pictures, it was logical to expect a negative reaction to the cutaneous test. Allergies of the skin to colored print are known. Real, specific allergies are also known in which the reaction to cutaneous testing is negative.

The only practical therapy in the war economy in which the patient lived was to remove the source of trouble. He was ordered to read only black and white comics.

Correspondence

SNELLEN SYMBOLS AND THE NAVAL EXAMINER

To the Editor:—With regard to the letter of Lieut. Col. Edwin N. Beery in the June issue (ARCH. OPHTH. **29:** 1025, 1943), it is true that were the naval examiner to go beyond the notation 20/400 (1/20) he would necessarily have to modify his designation of visual acuity. That is, he would have to revert—in the instance cited—to the use of unity as expressed in 80/80 rather than 20/20; in other words, 5/400 reduced to 1/80 has a corresponding unity of 80/80. As previously pointed out, unity here has the same subtending angle of 5 minutes of arc as that indicated by the standard norm of 20/20.

Granting any such modification, however, it becomes apparent that this scale of visual symbols in effect can no longer obtain. Hence it may be seen that, although convenient for the special purpose it serves, this method is definitely restrictive in scope and does not take into account the larger visual angles as subtended in the lower visual brackets, and for this reason can be made to apply only to a selective group capable of more or less qualitative visual acuteness.

Properly to interpret the modus operandi of this procedure, it must be borne in mind that one is dealing with a fixed number of values, each being actually an integral unit of the whole and all falling of necessity within certain prescribed limits. In short, with a given distance of 20 feet (610 cm.), there is a total of 20 foot units, that is, a range of 20 to 1 or 1 to 20, and visual acuity as denoted by successive units is expressed accordingly: 20/20, 12/20, 6/20 and so on to 1/20, or, conversely 1/20 and so on to 20/20.

Finally, an acceptable formula for conversion of any visual symbol into its equivalent should be based on recognized and proved principles rather than on hypothetic or arbitrary grounds.

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J. A. C. GABRIELS, M.D., Albany, N. Y.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Teaching Affiliation of New York Eye and Ear Infirmary.—Teaching has been going on at the New York Eye and Ear Infirmary since 1824, at which time an act of legislature was passed requesting the New York Eye and Ear Infirmary to accept for ophthalmic teaching one physician from every county in the state of New York. In the more recent past, Dr. John Weeks and Dr. George Dixon developed the teaching, and from this nucleus a group of the board of surgeons of the infirmary banded themselves into a postgraduate school. The courses varied in duration from an intensive course of one week to a more or less prolonged course of several months.

The postgraduate and resident training at the infirmary has been under the auspices of Columbia University so far as the basic training courses were concerned for the past several years. In the very recent past, several of the infirmary residents have been granted the degree of doctor of medical science by Columbia University. It was the thought of the board of directors that all postgraduate teaching should be under university auspices so that the standards of teaching and the qualifications of the students would maintain a satisfactory rating.

The teaching group provides for instructions at the infirmary by members of the staff who have a teaching "bent." Dr. Conrad Berens has been elected as executive officer and clinical professor of ophthalmology and Dr. J. Morriset Smith as executive officer and professor of clinical otolaryngology. These officers are to recommend to the university other members of the teaching staff for appointments to their appropriate rank. The dean of Columbia University College of Physicians and Surgeons or his representative is to be ex-officio a member of the teaching committee of the infirmary, so that he can confer with the other members of the board concerning the teaching program.

It is felt by the board of directors and by the board of surgeons that this liaison will increase the teaching efficiency of the infirmary and will allow an ever increasing number of qualified postgraduate students to benefit from the program.

The resident staff is to continue the present basic science course at the Medical Center. It is hoped that increased research facilities will also be made available at the infirmary. A more coordinated course of postgraduate lectures is being developed, in which the facilities of the Eye Institute, Manhattan Eye, Ear and Throat Hospital and the infirmary will be amalgamated for a lecture program.

JOHN P. RUPPE, M.D.

SOCIETY NEWS

Egyptian Ophthalmologic Congress.—The annual Congress of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, March 19 and 20, 1944, beginning at 9 a. m. The symposium will be on myopia.

Obituaries

CLIFFORD B. WALKER, M.D.
1884-1943

The death of Clifford Walker deprives the profession of ophthalmology of an extraordinary man. The terms "genius" and "modern Helmholtz" have been applied to him, and all who knew him recognized the peculiar relentless persistence with which he hunted the solution of any problem which caught his interest.

CLIFFORD B. WALKER, M.D.
1884-1943

Geniuses have this quality. Like many ophthalmologists, Dr. Walker had a strong mechanical bent, and it was not accidental that his outstanding achievements were the development of the technics of perimetry and the operation for detached retina. One can assume that he would have made valuable contributions to the solution of other problems, with which his original and busy mind was concerned at the time of his death.

Dr. Walker's reputation was international; his training was American. Born fifty-nine years ago, in Cambridge, Vt., he was graduated from the University of California and Johns Hopkins University School of Medicine. He taught at Harvard Medical School, where he had a long association with Harvey Cushing. Later he became a professor at the University of Southern California School of Medicine. He contributed largely to the literature of ophthalmology and in 1913 was awarded the Knapp medal for ophthalmic research.

CARL FISHER.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

LIPOID DEGENERATION OF THE CORNEA. H. C. DONAHUE, Am. J. Ophth. **25:** 261 (March) 1942.

Donahue discusses fat metabolism and reports the case of a 32 year old white man who suffered progressive loss of vision but no other ocular symptoms. Examination of the eyes disclosed vision in each to be 20/70, unimproved with lenses. Each cornea was of normal size and curvature, with normal epithelium, but the deeper layers were almost completely opaque save for a 1 mm. band about the limbus and a 2 mm. central disk-shaped area which was comparatively clear. The opacity consisted of a solid, plaquelike, yellow, more or less homogeneous fatty tissue with several vertical folds seen grossly. No view of the iris was obtainable and only a faint red fundus reflex. All clinical and laboratory tests gave normal results, and roentgen therapy was unsuccessful.

W. S. REESE.

USE OF RIBOFLAVIN IN TREATMENT OF CORNEAL DISEASES. K. W. COSGROVE and P. L. DAY, Am. J. Ophth. **25:** 544 (May) 1942.

Cosgrove and Day give the following summary of their experiences with riboflavin:

"In 28 cases, corneal disease has been treated with riboflavin, with varying results. The cases of interstitial keratitis associated with hereditary syphilis responded more rapidly with the administration of riboflavin than when antisyphilitic treatment alone was given.

"Various corneal diseases recovered more rapidly under this treatment. Allergic cases and linear keratitis showed no improvement."

W. S. REESE.

SURGICAL REMOVAL OF CORNEAL SCARS. W. M. JAMES, Am. J. Ophth. **25:** 672 (June) 1942.

James gives the following summary:

"1. The history of the surgical removal of opaque corneal tissue has been reviewed, together with the description of the operative technique developed and advocated by Wiener. The advantages, difficulties, and dangers of the procedure have been presented.

"2. The preliminary infiltration of the corneal stroma with air before resecting the opaque tissue is, I believe, an original procedure. The separation of the lamellar planes of the substantia propria by the injected air makes the actual dissection much easier, and lessens the danger of accidentally entering the anterior chamber.

"3. A series of 10 patients, a total of 12 eyes, is reported. In 10 of the 12 eyes the visual acuity was improved following corneal resection. The pain of an advanced epithelial dystrophy was relieved after removing the diseased corneal tissue."

W. S. REESE.

General

STERILIZATION OF SHARP INSTRUMENTS BY CHEMICAL SOLUTIONS. M. H. POST and W. MOOR, Am. J. Ophth. **25:** 579 (May) 1942.

Post and Moor conclude: ". . . . to judge from the experiments herein reported, and from our clinical experience, we believe that five minutes' exposure

to the action of the solution reported as No. 4 [cresol 8 cc., oil of lavender 2 cc., thymol 2 Gm. and ethyl alcohol U. S. P. 88 cc.], in this series is sufficient for complete sterilization, though longer periods obviously increase the factor of safety without injury to the instruments."

W. S. REESE.

General Diseases

OCULAR PEMPHIGUS AND ITS RELATION TO PEMPHIGUS OF THE SKIN AND MUCOUS MEMBRANES. J. V. KLAUDER and A. COWAN, Am. J. Ophth. **25:** 643 (June) 1942.

Klauder and Cowan discuss pemphigus of the conjunctiva from a dermatologic as well as an ophthalmologic viewpoint. In particular, they review the interrelation of ocular lesions, lesions of the mucous membrane and cutaneous lesions. They report 12 cases.

W. S. REESE.

Injuries

OLD AND NEW IDEAS IN THERAPY OF CAUSTIC BURNS: REPORT OF CASES. O. THIES, Klin. Monatsbl. f. Augenh. **106:** 47 (Jan.) 1941.

Referring to previous publications on the treatment of caustic burns of the eye, Thies discusses mainly the transplantation of mucous membrane from the lips. He points out the symptoms indicating the necessity of transplantation in 11 cases of especially severe burns treated during the previous two years.

Transplantation was not done immediately in those cases in which, even in the presence of severe burns of the conjunctiva and changes in the cornea, the conjunctival vessels could still be traced and sensitivity of the cornea was fully preserved. The operation was performed as soon as possible in the absence of corneal sensitivity. The best time for transplantation of mucous membrane from the lip was during the first seven hours after the accident. Necrosis of the elevated portion of the chemotic conjunctiva could be observed in some cases after a few hours. Early transplantation may be futile in the presence of extensive destruction of the lids. The supply of mucous membrane from the lips was insufficient for annular coverage of the defect on the eyeball in 3 cases. In these, Thies removed the necrotic tissue down to the sclera at the lower portion of the burn, and, after freeing the sclera from subconjunctival remnants at the upper portion of the burn, he closed the wound with sutures.

In agreement with Denig, Thies stresses the necessity of removing the "depot" of the caustic substances between the conjunctiva and the sclera. The tissues in this area show serous edema in the beginning, but a more compact whitish substance later on, owing to the formation of alkali albuminates. Corneal complications, observed in almost every case, cleared after the operation, spontaneously in most instances.

Cataract was noted in 5 cases. This was of the type which follows an ammonia burn, described by the author previously. Granulations developed in 1 case at the upper portion of the burn, which had not been covered by the transplant, whereas they were absent in the lower, well covered area. Early cauterization is indicated, especially when an involvement of the cornea is beginning.

K. L. STOLL.

Instruments

A SLIT RETINOSCOPE: SLIT DISC FOR USE IN CONNEXION WITH MIRROR FOR RETINOSCOPY. M. KLEIN, Brit. J. Ophth. **26:** 510 (Nov.) 1942.

The model described is similar to the original Priestley Smith mirror, differing only in that both the plane and the concave mirror are two sided, one side of each being covered with a disk in which there is a narrow oblong aperture.

The disk can be revolved so that the aperture can be made to run in any direction. The disk-covered side thus becomes a narrow oblong mirror reflecting a strip of light the direction of which the examiner can turn in any meridian by revolving the disk. The article is illustrated.

W. ZENTMAYER.

Lids

ESTROGEN THERAPY IN EDEMA OF LIDS DURING MENSTRUAL AND CLIMACTERIC PERIOD: REPORT OF CASES. R. GUTZEIT, Klin. Monatsbl. f. Augenh. **106:** 477 (April) 1941.

The author reports favorable results obtained with estrogen given by mouth and applied locally in the form of salves in 3 patients suffering from edema of the lids during menstruation or the menopause. He used salves containing dioxyldiethylstilbene and estrone. Estradiol benzoate dragées were given to 1 patient and solution of dioxyldiethylstilbene to another. The use of estrogen for edema of the lids is sometimes advisable long after cessation of the menses.

K. L. STOLL.

Neurology

SUPRASELLAR ANEURYSM: REPORT OF A CASE, WITH RECOVERY. R. M. KLEMME and R. D. WOOLSEY, Arch. Neurol. & Psychiat. **47:** 662 (April) 1942.

The authors report a case of suprasellar aneurysm exposed and incised at operation. Aneurysms of the infraclinoid portion of the internal carotid artery are well known to have associated with them paralysis of the third, fourth, fifth and sixth cranial nerves. The symptoms which distinguish the supraclinoid, or suprasellar, aneurysm are chiefly interference with the optic tracts and with the visual fields. In the case reported, examinations of the visual fields over a period of five years provided a record of slow growth of an aneurysmal sac with gradual encroachment on the optic nerves. These fields provide the most important feature of what Jefferson has called the characteristic picture of a supraclinoid aneurysm, i. e., rapidly failing vision in the ipsilateral eye with a superimposed definite homonymous hemianopsia in both eyes. Another interesting finding was a large homonymous field defect associated with atrophic nerve heads. The visual acuity of the left eye could not be measured. The patient could only occasionally distinguish light. The authors comment that this is a feature common to the picture of supraclinoid aneurysm and quote from Jefferson's monograph that "a homonymous field defect with papilledema is a neurological commonplace; the case is far otherwise when the nerve heads are atrophic."

R. IRVINE.

OPHTHALMOLOGIC AIDS IN NEUROLOGIC DIAGNOSIS. I. GIVNER, Arch. Neurol. & Psychiat. **47:** 1067 (June) 1942.

The author calls attention to ocular signs in four relatively uncommon syndromes involving the central nervous system.

"1. Association of sclerosis of the cerebral basal vessels with optic nerve atrophy and cupping of the optic disks.

"2. Retinal changes in tuberous sclerosis. Observations were made on a 5 month old infant, the youngest patient to be reported on while still alive. General examination showed nothing to account for convulsions until a study of the fundi was made. The appearance both of the retina and of the optic disks has changed during two years of observation in that a new lesion has appeared in one eye and the associated edema in the opposite disk has extended to involve the macula, giving a cherry red spot. An encephalogram taken after examination of the fundi showed the typical 'candle droppings' of the ventricle.

"3. Ocular changes in the postencephalitic parkinsonian syndrome, as observed in 17 consecutive cases. The following signs were emphasized: (*a*) Inability to use the accessory elevator (frontalis) muscle, varying in degree from complete inability to noticeable diminution in function. However, this muscle was brought actively into play at the time the eyes rolled up to fix. (*b*) Oculogyric crises. The influence of premotor cortical excision as performed by Klemme was observed. (*c*) Cogwheel movements of the eyes on looking from side to side. (*d*) Convergence insufficiency.

"4. Cyclic oculomotor paralysis, as observed in the 32 reported cases. In the case described the phenomena consisted of complete paralysis of the third nerve on the left side. The patient had ptosis and enlargement of the pupil on the left side; the pupil measured 8 mm. and reacted only sluggishly to light and consensually. After observation for one minute a little twitching arose in the upper lid, and gradually this became quicker and livelier, ending with complete opening of the palpebral fissure. At this moment the pupil contracted to 3 mm., while the normal, right pupil kept its usual size. After twenty seconds the left upper lid fell slowly, and at the same time the pupil again dilated. This cycle repeated itself at irregular intervals all day long. It occurred once or more during sleep, awakening the patient. During the spastic phase refraction showed an increase in myopia, of 2 D., indicating the association of the ciliary muscle in the spasm. Pupillographic examination by Dr. Otto Lowenstein gave the following responses:

"(1) The right pupil dilated slightly when the spastic phase involved the left eye. (2) Five seconds was required for the pupillary contraction in the spastic phase to reach its greatest intensity and nine seconds for the subsequent maximum dilatation. (3) The left pupil reacted to near point fixation to the extent of 0.3 mm. but did not react consensually until the diameter was 6 mm. or over.

"Oculomotor paralysis did not develop until the patient was 22 years old, a few months after resection of the levator muscle for the congenital ptosis which was a part of the complete paralysis of the nerve."

R. IRVINE.

LISSENCEPHALY. A. E. WALKER, Arch. Neurol. & Psychiat. **48:** 13 (July) 1942.

A case of lissencephaly, or agyria, "unconvoluted cerebral hemispheres," is reported. Clinically a diagnosis of glioma of the retina with extension to the brain was made. Autopsy proved the condition to be congenital malformation of the eyes and central nervous system. The ocular anomalies represented an arrest of development at approximately the fetal age of 3 months, with superimposed abnormal development of tissue, giving a curious mixture of hypoplasia and dysplasia. There were microphthalmos and congenital malformation of the retina on the right, intrauterine secondary glaucoma on the left, hydrophthalmos, congenital cataracts, bilateral posterior synechias, bilateral bronchopneumonia, capillary hemangioendothelioma on the skin of the buttocks and lissencephaly.

A complete gross and microscopic study of the eyes and brain is reported.

R. IRVINE.

Pharmacology

FURTHER STUDIES CONCERNING HOMATROPINE CYCLOPLEGIA AND PAREDRINE, WITH SPECIAL REFERENCE TO THE RATE OF ACCOMMODATIVE RECOVERY. W. F. MONCREIFF and K. J. SCHERIBEL, Am. J. Ophth. **25:** 839 (July) 1942.

Moncreiff and Scheribel present the following summary and conclusions:

"Further studies on carefully selected patients show good clinical evidence that the rate of recovery from homatropine cycloplegia is not hastened by the action of paredrine. Additional evidence is also presented that the efficiency of homatropine cycloplegia is not enhanced by paredrine.

"In a series of 10 patients, the action of 2 drops of 5 per cent homatropine was found not to be superior to that of 6 drops of 2 per cent homatropine with regard to either the efficiency of the cycloplegia or the rapidity of recovery."

W. S. REESE.

The Pupil

CONTRIBUTIONS TO THE PHYSIOLOGY AND PATHOLOGY OF THE PUPIL: III. THE LATENT PHASE OF THE LIGHT REFLEX IN THE NORMAL HUMAN EYE. H. MACHEMER, Klin. Monatsbl. f. Augenh. **106:** 385 (April) 1941.

Machemer examined 150 pupils in healthy persons and patients for the purpose of analyzing and measuring the first phase of the light reflex of the pupil. Over 600 of the measurements taken were used for his thesis. He describes his own method of taking motion pictures of the pupillary reaction. He obtained thirty to eighty pictures per second.

He found in the normal pupil a more or less constant latent phase of the light reflex of 0.217 second. The range was 0.20 to 0.22 second. Adaptation of the retina, original width of the pupil, color of the iris, refraction and vision, age of the examined person and illumination had no influence on the duration of the latent phase, nor did fatigue. The reflex blinking which occurs occasionally after illumination of the pupil showed a decidedly shorter period of latency than the contraction of the iris muscles, namely 0.06 to 0.09 second. The blinking preceding illumination did not influence the duration of the latent phase of the contraction of the pupil.

The latent phase of the light reflex lasts 0.187 second in rabbits. Pictures, tables and bibliography are appended.

K. L. STOLL.

CONTRIBUTION TO PHYSIOLOGY AND PATHOLOGY OF THE PUPIL: IV. SO-CALLED PRELIMINARY ENLARGEMENT OF PUPIL DURING LIGHT REFLEX. H. MACHEMER, Klin. Monatsbl. f. Augenh. **106:** 398 (April) 1941.

Machemer refers to Byrne, who in 1922 found that sudden illumination of the pupil causes a dilatation followed by contraction. He called this phenomenon "preliminary dilatation." The author's research was undertaken to prove or disprove Byrne's contention that the preliminary dilatation of the pupil is an essential phase of the light reflex. From his experiments he concluded that preliminary dilatation of the pupil is caused by undulation of the width of the pupil resulting from its unrest. The undulations are due to motion of the iris prior to the light reflex and continue during the latent phase. The so-called preliminary dilatation does not represent a phase of the light reflex, nor is it a "psychosensory" reaction. Machemer recommends that the term "preliminary dilatation" be abandoned.

K. L. STOLL.

Retina and Optic Nerve

LIPEMIA RETINALIS. S. H. MCKEE, D. R. WILSON, A. F. FOWLER and B. WILEN, Am. J. Ophth. **25:** 513 (May) 1942.

The authors give the following summary:

"A case of lipemia retinalis in a 23-year-old male diabetic is reported.

"The plasma lipids on admission were 8.439 per cent.

"Associated with the lipemia there were (1) a moderate acidosis, (2) multiple xanthomata, (3) carotinemia.

"Detailed studies are presented, showing the correlation between the daily observations of the disappearance of the lipemia retinalis and the levels of the various components of the plasma lipids.

"We believe this case to be the sixtieth reported in the literature."

W. S. REESE.

FAMILIAL DEGENERATION OF THE MACULA LUTEA. J. W. CRAWFORD, Am. J. Ophth. **25:** 525 (May) 1942.

Crawford reviews the literature on familial macular degeneration and reports 8 cases observed for a number of years. He believes that the onset of puberty it not a causative factor, as the degeneration in 7 of his cases appeared between the ages of 5 and 8 years.

W. S. REESE.

PAPILLEDEMA WITHOUT INCREASED INTRACRANIAL PRESSURE. A. J. BEDELL, Am. J. Ophth. **25:** 685 (June) 1942.

Bedell notes the difficulty of determining the cause of papilledema. He presents an illustrated report of 6 cases, in 4 of which the involvement was unilateral, as a clinical photographic contribution to elicit discussion regarding diagnosis and to prove the value of colored stereoscopic photographs of the fundus in differentiating papillitis from papilledema.

W. S. REESE.

TREATMENT OF SYPHILITIC PRIMARY OPTIC ATROPHY. J. E. MOORE, R. D. HAHN, A. C. WOODS and L. SLOAN, Am. J. Ophth. **25:** 777 (July) 1942.

From this study of 250 cases it is concluded that routine therapy with the trivalent arsenicals and bismuth is valueless, and that the Swift-Ellis technic should be abandoned, but that syphilitic primary atrophy of the optic nerve can probably be prevented by the adequate routine treatment of early syphilis. Fever therapy is the only efficacious method of treatment.

W. S. REESE.

Vision

NIGHT VISION IN THE ARMY. B. W. RYCROFT, Brit. M. J. **2:** 576 (Nov. 14) 1942.

The examination of night vision among troops should provide the following information for the unit commanders: (1) the general state of night vision in the unit as a whole; (2) the names of men whose night vision is above average and who are thus fitted for particular services; (3) the names of picked drivers whose night vision is above average, and (4) the names of drivers whose night vision is defective and dangerous.

In the examination the author uses a so-called army night vision test, in which the test object is a large V mounted in five different positions on a translucent screen, behind which is a small bulb run from a dry battery and controlled by a rheostat and voltmeter. The lamp is at varying distances from each of the five screens, which are arranged as an irregular pentagon. The whole apparatus can be rotated so as to bring one screen at a time in front of the subject. The subject sits at 1 meter from the apparatus and is rendered fully dark adapted by wearing dark goggles for thirty minutes; then these goggles are cleared of moisture and the test is made. If all of the five V's are seen the night vision is excellent; and if all of them are missed it is very bad. The soldiers are divided into three classes with respect to night vision: above average, average and below average. Those whose night vision is defective are grouped according to age, status of day vision, intelligence and, finally, "no explanation." It has been found that poor results are normal in soldiers over the age of 30, especially if combined with defects in day vision. Frequently a soldier does not cooperate because he does not understand the tests, and those who wear spectacles always show defective night vision.

Up to date 10,000 men have been examined. The author believes that tests of the night vision as a basis for practical recommendations to unit commanders increase the efficiency of night operations.

ARNOLD KNAPP.

Vitreous

MOORE'S SUBJECTIVE "LIGHTNING STREAKS." F. H. VERHOEFF, Am. J. Ophth. **25:** 265 (March) 1942.

Verhoeff draws the following conclusions:

"Moore's subjective 'lightning streaks' are observed by many patients with numerous senile vitreous opacities. Not infrequently such patients fail to mention the streaks until specifically questioned.

"The streaks are elicited only by ocular motion.

"In most cases they are referred only to the temporal field, but exceptionally, in the same case, a streak may be referred to the upper, lower, or nasal field according to the direction of ocular movements.

"The patient probably is not actually certain from which eye the streaks arise, but guesses this correctly since they appear to be most conspicuous on the same side as the affected eye.

"The streaks are dependent upon separation of the vitreous. A streak is produced when an ocular movement causes a sudden impact of the shrunken vitreous upon the peripheral retina.

"The associated apparent increase in vitreous opacities is due to the concentration of the previously existing opacities into the smaller space occupied by the shrunken vitreous.

"The predominance of the streaks in the temporal field is probably due to the fact that this field extends farthest to the periphery, and is also due to asymmetry of the vitreous body.

"The streaks are of slight, if any, prognostic importance." W. S. REESE.

Society Transactions

EDITED BY DR. W. L. BENEDICT

AMERICAN OPHTHALMOLOGICAL SOCIETY

ALLEN GREENWOOD, M.D., *President*

EUGENE M. BLAKE, M.D., *Secretary*

Seventy-Eighth Annual Meeting, Hot Springs, Va., June 1-3, 1942

George Berkeley and "An Essay Towards a New Theory of Vision." DR. BURTON CHANCE, Philadelphia.

This article was published in full in the April issue of the ARCHIVES, page 605.

New Cross Cylinder Test of Astigmatic Axis for Use Without Test Type. DR. WILLIAM H. CRISP, Denver.

Every test, whether subjective or objective, for astigmatism proves at times inconclusive.

Any supposed infallibility of retinoscopy is vitiated by the varying refraction of different parts of the pupil and the impossibility of knowing exactly how large an area of the pupil is habitually utilized for sharp central vision. The retinoscopic finding is not final and requires revision at the trial case for almost all patients. The cross cylinder test for axis is more completely dependable than use of astigmatic dials designed for indication of the axis.

Some patients' judgment may be biased by the influence of individual shapes of letters. Beach's maltese cross test aims to meet this difficulty. In an effort to obtain an additional check in testing such patients I have found it effective to make use of the distortions produced by such an astigmatic axis dial as that of Lancaster and Regan or that of Verhoeff by using the manipulation of the cross cylinder which is commonly applied to the letter chart in testing the axis.

DISCUSSION

DR. WALTER B. LANCASTER, Dartmouth, N. H.: I cannot let an opportunity pass to express my appreciation of what I call a masterly presentation of how the problem of measuring refractive errors should be handled. I refer here to the methods rather than to the results. Ophthalmologists all have their own special ways of applying the principle. I want to mention only one. The speaker said that astigmatic dials frequently give misleading and unsatisfactory clues as to the axis, and any one who has used them knows that is so. I have found that one of the best ways of arriving at a more definite clue is the proper selection of the amount of fogging. One cannot use the astigmatic dials successfully if one allows accommodation to run rampant. One must use a strong enough positive lens to produce fogging. By varying the amount of fogging a little one gets different axes in a few patients, and the question is, What axis should be chosen? Suppose one concludes from various tests—including the record of previous glasses—that the true correction is approximately + 2 D. sph. ⊂ — 0.75 D. cyl., and one wishes to get a definite axis. Plus 2.25 D. gives one axis and + 1.75 D. in a few cases a different one. The proper strength sphere to use in fogging to determine the exact axis is the sphere which puts one end of the conoid of Sturm exactly on the retina, not a little in front or a little behind. This cannot be done with certainty at the beginning, because the examiner does not know the value of the sphere and the cylinder. Toward the end of the test, however, when he does know these values to

a close approximation, perhaps after measuring the sphere with both eyes and using the approximate cylinder correction he may make a final test for the axis with the sphere which equals the total correction in the strongest meridian. In the case just described (true correction, + 2 D. sph. ⊂ — 0.75 D. cyl.) the total sphere in the strongest meridian is + 2 D. Suppose it was not expressed as a minus cylinder, but as a plus (+ 1.50 D. sph. ⊂ + 0.75 D. cyl.). The total sphere in the strongest meridian would be 1.50 D. + 0.75 D., or 2.25 D. That is the sphere which brings one to the exact end of the conoid of Sturm. If it is a minus cylinder, the sphere is used as it is. If it is a plus with a plus, one adds the two and the result gives the proper fogging for the exact axis. With this method one will have somewhat fewer confusing findings.

DR. F. H. VERHOEFF, Boston: I have always relied on astigmatic dials as a means of arriving at a correct result. Of course, it is believed, although it may not be strictly true, that an astigmatic correction that is best for reading test letters is best for all other purposes. The final test of astigmatism, therefore, is the ability to read test letters. Astigmatic charts, cross cylinders and so on, provide a simple and rapid way of reaching the last stages of the final test. As a rule, I find I cannot improve by means of test letters the correction I quickly obtain with astigmatic charts. If one relies on test letters alone, the patient becomes so fatigued that the results are inconsistent. My main reason for speaking now is to call attention to the fact that on my astigmatic charts the lines have never been as solidly black, and the paper on which they are printed has never been as white, as they should be. These charts were first printed over forty years ago and I believe are still made from the original plates. A photograph of one of my charts and one of another type in which the lines are much blacker and the paper whiter do not, therefore, provide a fair test of the value of the fine lines on my chart. The comparison should be made with the same kind of paper and the same blackness of the lines in the two charts. My charts, as furnished by the manufacturer, can be greatly improved by careful blackening of the lines with india ink.

DR. EDWARD JACKSON, Denver: The astigmatic chart is, as has been said, an approximate approach toward the meridians. An approach that is more nearly final in that it simplifies the problem of the observer—the patient is making the observation—is to reduce the astigmatic chart to its simplest form of three lines in one direction and three lines in the other. This sort of a chart is to be rotated in any direction, and in using such a test object with the cross cylinder I have found this: The three lines at right angles to one another provide the best means of comparing the different meridians.

DR. FRANK P. SMART, Norfolk, Va.: There are two points I want to mention. The first is that in the original paper all the illustrations showed the dial placed above and in front of the test letters, the twentieth or the fifteenth line of letters being left exposed. It seemed to me that the differences were as apparent in the test letters as on the dial face.

The second point is one on which I differ from Dr. Lancaster. I have found that whenever one gets the circle of least confusion off the retina, bizarre results ensue. If, instead of fogging, one keeps the circle of least confusion on the retina at all times, the most positive, rapid and accurate results are obtained from the use of cross cylinders, both as to the amount and as to the axis of the cylinderic correction.

DR. CONRAD BERENS, New York: I should like to ask whether there has been any question of including the smaller Beach test objects in these charts. When Beach brought out these test letters and characters they were so large that I could not obtain very good results. Later I used the Z and N and the maltese cross in different sizes to conform to visual acuity as good as 20/10. Using the Beach characters in that way I found them accurate and apparently more useful for the final determination of the astigmatic axis than the astigmatic dials. Has Dr. Crisp had the circles reduced in size so that he can compare his astigmatic dials with

the Beach test objects, which have been reduced in size on a chart printed by the American Optical Company?

Dr. William H. Crisp, Denver: Because the letter chart was in place, and also the maltese cross, which I printed myself in india ink and attached with rubber cement, I left them so that they could be compared. The camera does not record irregular astigmatism, and these tests are going to be used on patients who have irregular astigmatism; the photographs therefore may not tell the whole story as to the effect on the patient of the cross cylinder combination with the letters, the maltese cross and the astigmatic dial, respectively.

As to fogging, I find that at times fogging helps in the earlier stages, but my impression is that toward the end of the examination the patient gets the best results if the accommodation is relaxed without definite fogging.

Dr. Lancaster spoke about the conoid of Sturm. When I get down to the point at which I want the greatest refinement in testing, there is almost no conoid of Sturm.

Correction of Low Astigmatism. Dr. S. Judd Beach, Portland, Maine.

This article was published in full in the May issue of the Archives, page 775.

DISCUSSION

Dr. John Green, St. Louis: There is a wide variation of opinion as to the effect of uncorrected low errors of astigmatism on ocular comfort and general well-being. Some ophthalmologists cannot bring themselves to believe that low astigmatic errors give rise to symptoms; hence they disregard them altogether or are content with an approximation as to both amount and axis. To many patients these approximations are satisfying. It is my contention that the examiner should have sufficient pride in his work to endeavor to perform a precision job on every one of his patients.

It is my practice to correct fully high astigmatism. But there are exceptions. When the prior correction has been a sphere or a spherocylinder, it seems best at first to undercorrect the astigmatism, lest the patient, because of the distortion of objects or a sense of dwarfism or gigantism, discontinue the use of the glasses.

I agree with Dr. Beach that patients differ completely in their reaction to the same amount of astigmatism. It is perhaps unimportant to insist on the constant wearing of low cylinders of equal strength and axis. On the other hand, it seems advisable to prescribe for constant wear corrections for astigmatic errors under the following four conditions:

1. When the astigmatism is equal but at different axes.
2. When there is a difference in the degree of astigmatism.
3. When the astigmatism differs in degree and is also at different axes.
4. When there is myopic astigmatism in one eye and hyperopic in the other.

Dr. Beach states that as the initial step he places in the trial frame the correction as estimated by retinoscopy and that this correction is made the basis for the subsequent procedure. Personally, I should prefer to arrive at a somewhat closer approximation by carrying out the familiar "round of the trial case," as advocated by Duane, using plus and minus 0.25 D. spheres and cylinders. It may be inferred —and correctly—that I am suspicious of the findings of the retinoscope and prefer to have these corrected or confirmed by subjective tests.

Dr. Beach points out that a patient resents additional fogging, which is implicit in the standard technic of adding plus cylinders either in the axis of the trial frame cylinder or at right angles to it. With this technic, the sphere being slightly overcorrected and the cylinder presumably of the proper strength, the patient is disconcerted to find that the next step is the placement of an auxiliary lens which deprives him of his 6/10 or 6/7.5 line of letters. He cannot understand why he is suddenly thrust back into a fog. To forestall the patient's unfavorable com-

ments, I frankly admit that the auxiliary lenses produce blur, but point out that it is his job to select the lesser of the two evils. At this point it does no harm to refer casually to the superior intelligence and extraordinary powers of observation of the patient. This enhancement of his ego is helpful in riveting his attention to the matter in hand.

Dr. Beach's method is acceptable to less intelligent patients who are annoyed by the overcorrection of the sphere. Their annoyance will not be increased by the addition of an auxiliary minus cylinder at the improper axis, and they will welcome the increased acuity when the added minus cylinder in the proper axis gives a clear indication as to increase or decrease of cylindric strength.

Dr. Beach offers, by means of subtraction technic, a method of determining the presence or absence of low astigmatism at the four cardinal axes. The inferences he draws from the several maneuvers described are sound and in accordance with accepted principles of optics. He depends for still more precise placement of the axis on the relative strength of the "signals" indicated by auxiliary minus cylinders. Does he in practice prefer this method to the well known and widely appreciated use of the cross cylinder for this purpose?

Assuming that the axis has been accurately determined and the strength of the cylinder fixed by standard technics, including the cross lines of the Lancaster or Camp-Thomas chart, is it possible to refine the estimation of strength to a still higher degree? I believe that it is. For this purpose I use a 0.06 D. cross cylinder (first suggested in 1932). This consists of a lens ground with a — 0.06 D. sphere on one side and a + 0.12 D. cylinder on the other. With a low hyperopic astigmatism, axis 90, which has been perfectly corrected, an observant patient will detect no difference in the sharpness of the smallest letters in the two positions of this cylinder. When the cylinder is placed with the plus axis parallel to the plus axis in the trial frame, the horizontal lines will appear sharper. With the minus axis thus placed the vertical lines will be better defined.

When one is using the 0.06 D. cross cylinder there must be no overcorrection of the sphere.

Rocking the cylinder, especially with low astigmatism, often fails to give any positive indication. With higher astigmatism it is useful, especially if the patient is permitted to do the rocking. A keen person can be incited to utmost effort by physically participating in the determination of his error. He is thus encouraged to work out his own salvation in partnership with the examiner.

It is indeed a pity that many examiners are wedded to a single method. In the determination of low astigmatism the examiner should have at his command the various technics, and should modify his methods in conformity with the mental and psychic peculiarities of his patient. Particularly is the neglect of astigmatic charts hard to understand. Granted that the dial is occasionally misleading, it is in most cases of the utmost value in determining the presence, the approximate axis and the strength of the correcting cylinder. It is remarkable and deplorable that few refraction clinics in this country are equipped with astigmatic charts.

I am indebted to Dr. Beach for presenting a refinement of refraction technic that is proving increasingly satisfying in practice.

DR. WILLIAM H. CRISP, Denver: Dr. Beach has properly called attention to the fact that in dealing with a patient with a low error of astigmatism it is rather easy to overlook an off axis. For tracing such fractions when other methods have not shown the presence of astigmatism, I use one of two methods, and I am apt to check one by the other. I should say that, instead of using four principal meridians I systematically use six, and instead of taking 90 and 180, and 45 and 135, I take 90 and 180, 30 and 120, and 60 and 150 degrees. I take a 0.12 D. cylinder, either plus or minus, and I hold it, for example, in the vertical or the horizontal position alternately, and over this simple cylinder I use a 0.12 D. or sometimes a 0.25 D. cross cylinder. The patient is asked to say whether the two

lines of the single cross are more nearly equal in one position of the cross cylinder or in the other. If I am adding plus to his plus vertically and he does not need more plus vertically, he will say the lines are more nearly equal with the minus of the cross cylinder placed vertically. If in each of the six meridians he rejects even 0.12 D. of cylinder, I may assume that there is no correctible astigmatic error.

I can do the same thing with the cross cylinder and the letters, running through the six meridians one after the other. If in this way I once get a start on a low astigmatic error, I can put in the frame a 0.12 or 0.25 D. cylinder and then proceed to test the axis. In this way it is often possible to pick up a low error at an oblique axis that could not be picked up in any other way.

Dr. Burton Chance, Philadelphia: While listening to the essayist I thought that if there was a guest listening who had been debating as to whether or not ophthalmology should be taken up, he might suddenly disappear because he had begun to doubt that he could ever prescribe a glass with which a patient would be happy. Helmholtz has been charged with having made the statement that the eye is a faulty instrument. In truth he did not so state; what he did say was that if one were to be offered an instrument having the optical defects inherent in the human eye, one would never accept it from the instrument maker. The eyes are organs capable of making their own adjustments, and it is impossible to treat them in the way in which one would operate a fixed instrument.

With reference to the necessity of correcting low errors: In perusing the early records of the late Dr. William Thomson, I have found that many a patient had been sent to him by Weir Mitchell because of minor nervous troubles. Not a few of his prescriptions, which both Thomson and Mitchell carried out with the greatest particularity, call for much less than 1 D. The letters sent by the patients to Thomson state that they had been made happy by their spectacles, with which they had been relieved of pains and other troubles not previously remedied.

Dr. C. A. Clapp, Baltimore: I should like to ask Dr. Beach one question: When I prescribe a 0.25 D. cylinder and the patient comes back with relief of headache and other symptoms, am I practicing ophthalmology or psychiatry?

Dr. F. H. Verhoeff, Boston: I presume that Dr. Beach carries out these procedures during cycloplegia and again after the cycloplegia has worn off. I should like to ask him whether he gets different results in the two sets of tests and, if so, which he relies on.

Dr. Nelson M. Black, Miami: I should like to ask Dr. Beach whether in correcting low degrees of astigmatism he applies the same method when the patient has presbyopia.

Dr. Alfred Cowan, Philadelphia: The thing I like about Dr. Beach's test is that he utilizes the ordinary test case lenses. There is no such thing as a human eye that is as mathematically exact as a schematic eye, and lenses which are given to a patient for the correction of a certain error are for the purpose of giving him comfort and relief. It is a different thing to prescribe glasses for a person whose vision is only 6/12 than for one, for instance, with 6/5 vision. The one with 6/5 vision will demand a much more nearly exact correction than the one with 6/12 vision. In a subjective test it is important that the correction be approximate before refinements are attempted. The best refractionist is the one who not only arrives at the proper conclusion but does so rapidly. For instance, in doing a retinoscopic examination it is wrong to start out with 0.50 D. differences. Rather overcorrect first and then undercorrect, and the result will be within 1 D. Not until then should fine differences be studied. It is up to the ophthalmologist to decide which test or tests are applicable to a particular patient. If all tests were used on each person, they would take three or four days. Dr. Beach brings out a test used with ordinary trial case lenses, and I think it is the proper procedure to utilize the resources of the ordinary trial case before any of the methods of refinement are attempted. The quicker one arrives at a near refraction, the better the refraction will be done and the better the patient will be satisfied.

DR. S. JUDD BEACH, Portland, Maine: The catholicity of the speakers has pleased me. I expected more prejudice in favor of particular tests. I appreciate what Dr. Green and Dr. Crisp said about various little modifications to improve this one. Very likely Dr. Crisp's use of six axes instead of four might be adopted in some cases to great advantage.

With regard to what Dr. Green said about the use of the cross cylinder, I am quite aware of all its merits and use it constantly. Just why it fails at times I do not know. Possibly changing the cylinder before the patients' eyes may disconcert them. There are probably other reasons. All the tests have their drawbacks.

In answer to Dr. Clapp, I think that Dr. Lancaster's remark that psychiatry and ophthalmology cannot be divorced is the best answer.

In reply to Dr. Verhoeff, I suppose I shall differ with a large proportion of practicing ophthalmologists in relying on the postcycloplegic examination when its result differs from the cycloplegic.

I should answer "Yes" to Dr. Black's question, although I do not carry through to the prescription.

Until this year I agreed perfectly with Dr. Cowan's belief that one can ignore the refinements in an eye with low vision. In general, tests not quite so refined have been satisfactory in the examination of amblyopic eyes, but I have 2 patients with vision around 6/30 who are highly sensitive to cylindric correction.

Practical Importance of Aniseikonia. DR. EDWARD JACKSON, Denver.

The nature and importance of aniseikonia were described and illustrated by 3 cases of an extreme form. One was the case of Sir George B. Airy, reported in 1827. In the other 2 aniseikonia followed the extraction of cataract from one eye while the other eye retained useful vision. These cases indicate the possibility of new visual coordinations, which may be formed even late in life.

Reply to Criticisms of Aniseikonia. DR. WALTER B. LANCASTER, Hanover, N. H.

Heterophoria, especially anisophoria, is a source of error.

Peripheral fusion, which is depended on in the measurement of aniseikonia with the eikonometer, is unreliable in the presence of central images which, though dissimilar, have a tendency to become fused or alined.

Findings with the frontal plane horopter and with the grid-nonius horopter were discussed.

Enormous size differences occur in the normal use of the eyes, e. g., asymmetric convergence.

In use of the eyes on small objects, differences in size would be below the threshold of vision, and yet use of the eyes for near vision is said to be more often a cause of symptoms than use for distant vision.

DISCUSSION OF PAPERS BY DR. JACKSON AND DR. LANCASTER

DR. H. BURIAN, Hanover, N. H. (by invitation): In connection with Dr. Jackson's paper, I should like to mention the following facts: It is true that one may become accustomed to the wearing of glasses which at first cause certain distortions of space, and one might well assume that once one gets accustomed to such distortions the glasses are satisfactory and no further therapeutic procedures are needed. However, the visual act consists of two phases, or aspects. One consists of the acquired clues, represented by such monocular clues as perspective and shade. The other consists of those clues which are innate and based on incongruity of the ocular images. By wearing lenses involving considerable size differences — 3, 4, 6 and 8 per cent—for some time I was able, after a few days, to accustom myself to them in the sense that I no longer saw the desk top tilted or other distortions in space. However, when there were no clues to perspective in the field of vision the

size effect returned. The experiments were strenuous, and have taken up most of my time during the last two or three years, and I am looking forward to publishing them some time. The main result was to show that, while one apparently becomes accustomed to certain inequalities in ocular images one does not actually become accustomed to them, because one cannot change one's disparities. What one can change is that part of the visual apparatus which is acquired by experience—which has been learned.

In amplifying some of Dr. Lancaster's statements, I should like to show a slide in which measurements taken on 107 flight cadets, 341 college students and 100 clinical patients referred because of aniseikonia are presented. This slide is most revealing. It shows that in the flight cadets—young men who were highly selected—the amount of aniseikonia actually measured with the eikonometer was small. Of the cadets, 93 per cent showed an aniseikonia of 0.5 per cent or less, and only 1 had an aniseikonia of 1 per cent. Among the college students, who were healthy young men with relatively few ocular complaints, the amount of aniseikonia was considerably higher. The percentage of those measuring 0.5 per cent or less dropped to 33. The picture was entirely different with the clinical patients, who came with complaints. Only 15 or 16 per cent showed an aniseikonia of 0.5 per cent or less; the vast majority had an aniseikonia considered of clinical importance. These figures are of interest so far as they answer objections raised with regard to certain clinical aspects of aniseikonia. The fact that the majority of the patients referred for an examination showed a much larger amount of aniseikonia than is to be found in normal persons in itself justifies the endeavor to correct this anomaly, especially if previous attempts to relieve the patient by other methods have failed. The figures also clearly indicate that the favorable results achieved with aniseikonic corrections on the basis of painstaking measurements cannot be explanied away by the suggestive influence of the examination or the unusual glasses.

As to the last point, which I should like to have Dr. Lancaster amplify, there is an even more convincing argument. Among numerous patients who have been reexamined over a period of from five to ten years, in many the amount of aniseikonia varied only within the limits of error of the method. In others there were some changes, which were, however, most frequently attributed to changes in the refractive correction needed. Such a stability of measurements can occur only when a physiologic but not a psychologic factor is concerned.

Finally, there is a point I should like to raise in connection with Dr. Jackson's interesting case of aphakia. Naturally we at Dartmouth have been most interested in unilateral aphakia and have examined a great number of patients with this condition. By putting on a refractive correction, an occasional patient may secure binocular single vision, but only in a small area around the fixation point. On the other hand, we have always been able to restore binocular single vision over the whole field if the aniseikonia was measured and corrected, except when some other difficulty intervened, such as the presence of strabismus. It is important that the aniseikonia be corrected a year or so after the loss of the lens; otherwise the dissociation that sets in results in a divergent strabismus. We have usually worked with younger persons, because we do not think it worth while to work with older subjects, who are usually happy without binocular vision.

A second point is that the refractive and aniseikonic correction cannot be combined in a single lens in cases of unilateral aphakia, because of the enormous size difference. The resulting spectacles are unsightly and have poor field qualities. We have, therefore, in such cases resorted to the prescription of contact lenses; by computation of the curvatures and the thickness of these lenses, the size difference as well as the refractive error can be corrected. Professor Ogle has reduced the somewhat complicated computation to nomographs which can easily be handled by an assistant.

A by-product of our work with contact lenses in cases of unilateral aphakia, as well as other cases of aniseikonia, is the light thrown on the problem of aniso-

phoria as opposed to aniseikonia. With the contact lenses not containing the correction for aniseikonia, the patient measures a certain amount of size difference. If the contact lenses are now properly computed from the aniseikonic data, the patient should have no aniseikonia. There would be no possibility for refractive lenses introducing a differential prismatic effect. Such cases have actually been encountered at the Dartmouth Eye Institute and have further strengthened the conviction that a size difference, not an anisophoria, is being measured by the eikonometer.

DR. CONRAD BERENS, New York: I shall first say a word about Dr. Jackson's experience. For a good many years I was deeply interested in seeing whether I could add to the comfort of patients who had had cataract removed from one eye by giving them single binocular vision and good amplitude of fusion. I did obtain binocular vision and some fusion, but as a rule the patient became uncomfortable after a short time and gave up the idea of fusion. One patient, a woman who was anxious because her eye tended to "wander out," exercised for three or four months. The orthoptic technician said she was making a mistake, but she wished to continue. She persisted and did obtain some fusion, but she has since neglected that eye. I found that when the lenses were centered lower, she was somewhat benefited. In the last three years I have seen patients in New York and at Dartmouth who have worn contact lenses with iseikonic lenses, but I have found that even they are not entirely comfortable. Therefore, I usually tell the patient before extracting a cataract that if the other eye has good visual acuity he may be made uncomfortable and may continue to be so.

I thought it might be of some interest to compare the study of 450 patients examined during the last year with a previous study. In the latter, 75 per cent of 502 patients who wore their iseikonic correction reported partial or complete relief from unpleasant symptoms. Of the 450 patients seen during 1941, 32 had incomplete ophthalmo-eikonometer examinations. One of the most difficult patients is the one whose visual acuity in one eye is too low to be tested. There was no appreciable aniseikonia in 122 patients. Aniseikonia was present in, but no iseikonic prescription was given to, 50 patients. An iseikonic prescription was given to 33 who did not have it filled. Iseikonic corrections were worn by 29 patients who did not report on the results. Iseikonic corrections were worn with no improvement of symptoms by 38. In the remaining three groups in which iseikonic corrections were worn there was slight improvement in 33 patients, moderate improvement in 58 and marked or nearly complete relief in 55. In other words, of the 184 patients who wore iseikonic corrections and reported the results, 146, or 79 per cent, claimed they were benefited. In the previous group only 75 per cent claimed they were benefited. I believe this higher percentage of reported improvement may have been caused by several factors. First, the present examiner for the department of aniseikonia does not recommend correction so often; second, the ophthalmologists referring patients for examination select them more knowingly because of greater experience, and, third, the interval between the time when the lenses were obtained and the questionnaires answered was shorter. Some patients seem temporarily to be benefited and find later that iseikonic lenses may be discarded or ordinary lenses worn with comfort.

Unquestionably many patients can wear ordinary lenses or even wear no lenses and still not complain of symptoms although they seem to have the same refractive errors as patients who apparently require iseikonic lenses for relief of annoying asthenopia. Physical, psychologic and ocular factors which make these patients hypersensitive should be searched for and if possible eliminated.

DR. WILLIAM H. CRISP, Denver: I should like to know with regard to Dr. Lancaster's and Dr. Burian's work whether the test was made with or without cycloplegia.

DR. FRANCIS HEED ADLER, Philadelphia: May I ask Dr. Lancaster and Dr. Burian to show their slide again? To me it was not very convincing. The

group of flight cadets were separated from the group of normal students further than the clinical patients were. The flight cadets, being practically emmetropic, were free from aniseikonia, but the clinical patients, who had complaints, were similar to the 341 college students, who did not, and that to me is not convincing evidence that the difficulties of the patients were due to aniseikonia.

DR. J. S. FRIEDENWALD, Baltimore: Dr. Lancaster has referred to a small piece of work which I did a number of years ago, and I should therefore like to discuss some of the points he has raised.

Dr. Lancaster said that anisophoria has no bearing on the readings made with the eikonometer. In the early literature from Dartmouth, a great deal of emphasis was placed on a phenomenon closely related to heterophoria, to which Professor Ames gave the name "retinal slip." It is important to know whether Dr. Lancaster believes that the early work of Professor Ames was erroneous. On the other hand, if the early work on retinal slip is not to be denied, it follows that a patient whose heterophoria varies with the direction of gaze will give erroneous readings on the eikonometer. In the study which I reported six years ago it was found that the incidence and degree of "anisophoria" among office patients in Baltimore was approximately equal to the incidence and degree of "aniseikonia" among office patients at Dartmouth. It remains to be proved therefore, that any of the patients giving positive readings with the eikonometer really have aniseikonia. The issue could be simply settled if duplicate measurements with the eikonometer and with a phorometer at different directions of gaze were made on a substantial series of patients.

Dr. Lancaster places a great deal of emphasis on correlation between readings on the eikonometer and complex measurements of space judgment. The mechanism of space judgment remains obscure, and the habitual innervation of the eye muscles to various directions of gaze may play an important role in such judgment. It follows that a person with abnormal ocular motility, for instance with anisophoria, may make erroneous space judgments detectable with the tests which Dr. Lancaster has reported. An example of the role that innervation sense regarding the direction of gaze plays in space judgment is the fact that on asymmetric convergence, a normal person makes approximately correct space judgments, interpreting the disparity in his retinal images differently on lateral gaze and on looking directly ahead. Dr. Ames explains this by assuming a physiologic variation in perceived image size with asymmetric convergence movements. No evidence has been presented to substantiate his hypothesis, but if it is correct, it means that the perceived image size is intimately influenced by the innervation sense of the direction of gaze, which Dr. Lancaster denies.

The unequivocal measurement of aniseikonia is difficult. Some years ago Dr. Burian, of the Dartmouth staff, developed an instrument in which the patient was not required to make conjugate ocular rotation in order to make a reading. Criticisms of this instrument by Dr. Verhoeff have never been answered. However, analyses of paired readings on the Burian eikonometer and on the ordinary eikonometer have not been reported. If it could be shown that there is a close correlation between the readings with the two instruments, the Dartmouth theory might be strongly supported. If the readings with the two instruments were not generally in accord, one would be entitled to conclude that the ordinary eikonometer generally measures not aniseikonia but anisophoria.

DR. ROBERT H. COURTNEY, Richmond, Va.: Twelve years ago Dr. Cowan drew my attention to the fact that aphakic eyes with a high degree of astigmatism could be corrected better if they had a minus cylinder in the posterior chamber of the trial frame, combined with a plus sphere in the anterior chamber. This limits a patient's field of vision considerably, but it gives him a remarkable amount of comfort.

About a year later a patient consulted me because of poor vision in the left eye and headaches for which she had not been able to obtain relief. She had normal

vision in the right eye and less than 20/200 in the left eye. The left cornea was conical. The correction for the right eye was + 0.50 D. cyl., axis 90, but for the left eye it was + 4.50 D. sph. ⊃ —7.50 D., axis 95, which gave her normal vision. Doubting her ability to wear this correction, I asked her to stay in the office for a day's trial of these lenses. She wore them with perfect comfort. During the next few days I refined the correction according to Dr. Cowan's suggestion, and it then proved to be more satisfactory. There has been a gradual increase in the total correction in the left eye during the last ten years.

Conical cornea has appeared in the right eye, developing as rapidly as it had in the left eye. In spite of the high degree of astigmatism, the patient does her school work with perfect comfort for the better part of each year. Whether a contact glass would have prevented an increase of the conical cornea I do not know. The patient was well satisfied with the correction of her astigmatism in spectacles and did not desire the examination for contact lenses. Within the last two years ruptures of Descemet's membrane have developed, and the vision in the left eye cannot be improved to normal.

Dr. Burton Chance, Philadelphia: I wish to remind Dr. Jackson that there was an earlier case than that recorded by Airy. Pepys, the famous diarist, had much trouble with his eyes. It was believed that this was caused by the writing of his diary, but certain symptoms of which he complained were such as would now be attributed to inequalities in fusion. At one of his parties there were a number of medical men. Pepys asked one of them to explain whether it was really true that human beings see with only one eye, to which question he received the reply that they see with two eyes, which act together. But Pepys was not able to see equally well with his two eyes, and as presbyopia had come on, he could write only with a great deal of pain. He therefore ceased keeping his diary.

Dr. Edward Jackson, Denver: To discuss the discussion, I believe that it gives the impression that little is known of this work and nothing is known of the most important factor in vision—the development of neural and cerebral coordination and anatomy—concerning which even physics will not help. In such a case as that mentioned by Dr. Chance the subject is right eyed and does not know it, a situation indicating the importance of the psychology of vision, about which, I feel, there are impressions but little that can be called scientific observations.

Dr. Walter B. Lancaster, Hanover, N. H.: In reply to Dr. Crisp's question, I might say that there is on the staff at Dartmouth a man trained at Wills Eye Hospital; does that answer the question as to whether cycloplegia is used? He uses it ten times as often as I do.

It is apparent that Mr. Ames feels convinced of the soundness of his position—that the eikonometer measures aniseikonia, whereas, on the other hand, Dr. Friedenwald is not convinced that this is proved, but thinks anisophoria is the source of the errors recorded. My own position is this: Mr. Ames's claim that the standard eikonometer does measure aniseikonia is fully substantiated by a mass of evidence only a small part of which has been published. I have repeated many of the experiments myself. I have made tests on an apparatus which I devised to measure aniseikonia without the possibility of anisophoria entering into the problem, since the gaze is continuously in the primary position, with no shifting. This confirms me in my belief. It also answers Dr. Friedenwald's extraordinary statement: "It remains to be proved, therefore, whether or not any of the patients giving positive readings with the eikonometer really have aniseikonia."

The confirmation is a double one: It shows agreement in the measurements on the two types of eikonometer, and it shows that putting on aniseikonic lenses corrects the aniseikonia as measured on both instruments.

Moreover, I have measured patients for anisophoria with this and other devices. This apparatus was provided with small lights ("muscle lights"), one central and one 20 degrees from the center, to measure the muscular imbalance in the primary position, and 20 degrees right, left, up, down or oblique to measure

the anisophoria. I found that anisophoria was almost universal (as is aniseikonia). As stated in my paper, I regard a certain amount of anisophoria as natural and normal.

When one is measuring aniseikonia on the standard eikonometer, heterophoria may be troublesome if it is not corrected. It is not true that "it has no bearing on the readings made with the eikonometer," and if I said or implied that, I was wrong. One of the cases reported in the paper illustrates this very well. The magnitude of the aniseikonia as measured with and without correction of the heterophoria (usually by prisms) will differ materially.

In short, my conviction is that there is ample evidence for the existence and importance of aniseikonia and that the standard eikonometer makes valid measurements confirmed by use of the space eikonometer and numerous other crucial tests. On the other hand, I am convinced that anisophoria is common, but not usually a source of trouble, probably because so small a part of one's seeing is done outside of the central area, with a diameter of 15 degrees, within which anisophoria is markedly less than outside of it.

The magnitudes being measured by the eikonometer when compared with those measured by the phorometer are significant. A size difference of 1 per cent means 1 per cent of the distance from the center target to the dash 4 degrees away—1 per cent of 4 degrees is 1 per cent of 240 minutes, or 2.4 minutes. A letter on the 6/6, or 20/20, line subtends 5 minutes.

The difference which the patient has to detect in being measured for 1 per cent aniseikonia is 2.4 minutes of arc, or less than half the size of the 6/6 letters. That is why only persons with good visual acuity can be examined on the eikonometer and why poor observers are unsatisfactory patients.

Heterophorias, on the other hand, are usually measured in prism diopters (Dr. Friedenwald used prism degrees): 1 prism diopter equals about ½ degree, or 30 minutes of arc. Compare this with 2.4 minutes. In the measurement of heterophoria the unit is thirteen times as large as in the measurement of aniseikonia. All clinicians who have had experience with the eikonometer know that heterophoria affects the reading of the eikonometer, but that anisophoria is what is being measured is easily disproved. Moreover, aniseikonia readily explains certain phenomena of space perception which are not explainable without it and which are definitely not explainable on the basis of anisophoria.

Dr. Friedenwald makes light of the evidence from the space eikonometer, which is in favor, of findings with the standard eikonometer. Independent evidence based on data derived from entirely different and therefore independent methods of investigation seems to me the strongest and most convincing kind of evidence. The ground on which Dr. Friedenwald discounts this evidence is particularly weak. He says: "The mechanism of space judgment remains very obscure, and the habitual innervation of the eye muscles to various deviations of gaze may play an important role in space judgment." This is a surmise on Dr. Friedenwald's part, with little basis of fact. When I look to the right with my left eye covered, if my right lateral rectus muscle is paralyzed, I locate the point much farther to the right than it really is. I am guided by my innervational clues, and there is no question about the importance of innervational clues in such instances, but they do not suffice for the fine points of localization in normal eyes, and it is easy to cite cases in which they are even misleading. Thus a prism base will make one diverge one's eyes. Innervationally, divergence is associated with greater distance, yet objects usually appear nearer, not farther, with such a prism—a puzzle elucidated by Ames.

Recession of the Inferior Oblique Muscle at or Near the Insertion. DR. JAMES WATSON WHITE, New York.

Operations on the inferior oblique muscle done at the origin proved to lack modifications. A complete tenotomy gave in some cases the desired result, while

in others there was an undercorrection. This unreliability led to a myomectomy in which from 5 to 10 mm. of the muscle was resected. This operation gave more uniform results when a complete paralysis was desired. Attempts were made to get a partial effect by opening the muscle sheath and excising a portion of the muscle fibers. Later incisions were made on each side of the muscle as a partial tenotomy. These proved unsatisfactory.

In 1936, I receded the muscle at or near the insertion. This procedure proved so satisfactory that it has been used with increasing accuracy and confidence. The insertion is a cite of choice when one is resecting or receding an external rectus muscle if the convergent or divergent strabismus is associated with an overacting inferior oblique muscle of the eye to be operated on. A tuck at this cite made according to Wheeler's technic for tucking the superior oblique muscle has given less satisfactory results but is preferred to advancement over the margin of the orbit.

DISCUSSION

DR. JOHN H. DUNNINGTON, New York: It is always a pleasure to hear Dr. White expound on anomalies of the ocular muscles, for his advice is sound and his judgment is tempered by the wisdom of experience. The operation of recession of the inferior oblique muscle has intrigued me for two reasons: (1) tenotomy of this muscle at its insertion has not been a satisfactory procedure and (2) myectomy at its origin has produced inconsistent results.

I cannot agree with his statement that these two procedures produce similar results. In my hands tenotomy of the inferior oblique muscle at its insertion has caused almost invariably a complete paralysis of the muscle, paralleling in every way that rare condition congenital paralysis of the inferior oblique muscle. On the other hand, myectomy of the inferior oblique muscle at its origin has not abolished all upward movement in the nasal field—in fact, in some instances an upshoot has persisted in spite of the excision of 5 mm. of the muscle at its origin. In my opinion the failure of this operation to produce a complete paralysis is accounted for by the connection of the fascial bands with the inferior rectus muscle. The cut end becomes adherent at this point, thereby preserving some of the action of the muscle. This theory has been substantiated by the failure of surgical exploration to reveal any orbital attachment in many of the cases in which there is a persistent upshoot. Therefore, if, by receding the inferior oblique muscle a known number of millimeters one can avoid a complete paralysis, yet at the same time obliterate all overaction, definite progress will have been made. My experience with this operation is too limited to serve as a basis for a final appraisal, but my impression is that it has a genuine field of usefulness. I have done it only five times, and the patients have not been followed long enough for final judgment to be passed on them. I can say that in none has it produced a complete paralysis, and all have been benefited. I have used it only when the external rectus muscle had to be operated on at the same time. With this muscle reflected out of the way, recession of the inferior oblique is not difficult. Doing this operation on cadavers with the external rectus muscle *in situ* has convinced me that it is a much more complicated procedure than myomectomy.

The inferior oblique muscle is frequently adherent to the lower border of the external rectus as it passes underneath this muscle to reach its scleral insertion. The fusion of these two muscles at this point may lead to an unintentional and unrecognized severance of the oblique muscle in the course of a resection of the external rectus. I feel that such an injury to the oblique muscle accounts for some of the vertical deviations discovered after shortening of an external rectus muscle.

DR. LUTHER C. PETER, Philadelphia: If and when an external rectus muscle is detached to correct lateral deviation, the approach to the insertion of the inferior oblique muscle is quite simple. As Dr. White has pointed out, under such circumstances it is logical to tenotomize the insertion of the oblique muscle if this is indi-

cated. To make this approach under other conditions is inadvisable. The usual approach through the skin is accompanied by little trauma and by slight risk of infection as compared with operation on the insertion. It is true that tenotomy of the oblique muscle at its origin does not always yield uniform results, but this is true of any tenotomy, depending on the complete severance of all fibers. The same variation is equally applicable, under like circumstances, to the insertion of the oblique muscle.

Operation on the insertion of the inferior oblique muscle, when operative intervention is indicated, has for obvious reasons more to commend it than similar operation on the insertion of the superior oblique. In the first place, detachment of the superior rectus muscle becomes necessary—a questionable procedure—so that one may gain access to the superior oblique. Second, there is a definite anatomic connection between the superior rectus and the superior oblique when these muscles cross. This led Dr. Wheeler to advise rather free surgical intervention to produce the desired results, especially in shortening of the superior oblique muscle.

Those who do many operations for separation of the retina have realized the wisdom of Dr. White's procedure for use when the external rectus muscle must be detached. Under the proper conditions it is a worth while addition to operations on the inferior oblique muscle. Its choice emphasizes the careful selection of the proper muscle operation to accomplish definite ends.

It is gratifying to me to learn, from Dr. White's closing remarks, that he now recedes the inferior oblique muscle. It is evident to any ophthalmic surgeon who does many muscle operations that tenotomy of the vertically acting rectus muscle is not indicated. This is really a serious procedure, as is tenotomy of the oblique, unless one is dealing with an overacting oblique muscle and palsy of the superior rectus muscle. If one expects to get a full paralysis of the inferior oblique muscle —and apparently Dr. White's experience has led him to the conclusion that this is advisable, as has that of Dr. Dunnington—tenotomizing the tendon at its insertion will produce more nearly the desired result. I believe, therefore, that this is a definite indication for the operation which Dr. White has so well devised.

Dr. Conrad Berens, New York: I heard one of Dr. White's students speak of his suggested operation in 1936 or 1937. It was not until 1938 that I attempted this procedure, and since then I have performed unilateral recession of the inferior oblique muscle of only one eye in 8 cases, bilateral recession of the inferior oblique in 1 and operation on the inferior oblique combined with other operations in 2 cases. This is a total of 11 operations. Because of the importance of the new procedure, I have had my results analyzed to discover just what may be obtained from the operation without operation on the rectus muscles. I have done what Dr. Peter says one should not do and have found it not too difficult; that is, I have operated on the inferior oblique muscle without detaching the lateral rectus. By grasping the inferior oblique with a special muscle clamp, one can detach it at its insertion. When the muscle is completely detached, one may have trouble, because it is difficult to see where it was attached. A method which has been most satisfactory is to take a small tenotomy hook and lightly cauterize the sclera at the anterior extremity of the insertion of the inferior oblique muscle. In all but 2 of these operations nylon sutures (8-0) were used without reaction. Experimental studies with nylon suture material have been in progress for about a year. It apparently produces as little irritation as any suture material now available.

With regard to the results of tenotomy and myectomy of the inferior oblique muscle, which Dr. White has objected to, I have similar objections. One is that cyclotropia has developed in some patients. So far, among the 11 patients I have operated on by recession I have not observed serious cyclotropia. The greatest difficulty has been that I have not placed the inferior oblique muscle back far enough. I have receded it not more than 7 mm. and usually 5 to 7 mm. Unless the lateral rectus muscle is detached it is hard to work in the field involved, and that is

probably one of the reasons why I have found it difficult to recede the inferior oblique muscle more than 7 mm. When the lateral rectus muscle is detached, it is easy to suture the muscle as far from the insertion as one wishes.

Of the patients on whom I performed unilateral recession of the inferior oblique muscle, 5 showed marked improvement—from 4 to 6 prism diopters to a total correction of 18 to 20 prism diopters—which brings out the point which Dr. White made: It is still not known how far one should recede the muscle. None of these patients was amblyopic, and therefore the deviation could be measured carefully preoperatively and postoperatively. A patient who had bilateral hypertropia had insufficient correction. Two patients showed some increase of hypertropia. One of these was operated on again. The recession was somewhat small, (3 mm.), and later I performed myectomy of the inferior oblique muscle, with marked improvement.

It is interesting, as Dr. White pointed out and as Duane has stated, that there is a diminution of the lateral deviation with correction of the vertical imbalance. In the 8 patients whose inferior oblique muscle alone was operated on, there was a reduction of the horizontal imbalance (esotropia) from one third to one half of the deviation as measured with the screen test and square prisms.

In addition to the unilateral operations on the inferior oblique muscle there was 1 bilateral recession of this muscle—3 mm. on one side and 3.5 mm. on the other. The patient had left hypertropia of 25 prism diopeters and right hypertropia of 9 prism diopeters, reduced respectively to 6 prism diopters and 5 prism diopters. The lateral imbalance also improved, the esotropia decreasing from 18 to 5 prism diopters.

Two patients had multiple operations, including a recession of the inferior oblique muscle. One of these showed improvement in the hypertropia; the other had a transfer from right hypertropia to left hypertropia of the same degree.

From the work done so far in this particular field, I believe there is a tendency toward undercorrection by an average retroplacement of from 5 to 7 mm. The improvement of the lateral imbalance has been marked in most cases, a fact to be considered when one is performing this operation. I believe Dr. White has made an outstanding contribution to the surgery of the inferior oblique muscle.

DR. JAMES WATSON WHITE: I feel as Dr. Dunnington does about the effect of a myomectomy or tenotomy at the origin, but one should be careful that the paralysis of the superior rectus muscle is almost complete and that the upshoot is marked enough to warrant it. I have no statistics, but I have operated in many cases, and in the majority in which I judged I could do a myomectomy or tenotomy at the origin the correction has been satisfactory. In a comparatively few there has been an overcorrection, and I wish that in these I had receded the muscle. The first operation I did at the insertion was in the case of D.D., and I have not had a nicer result; so the muscle cannot be very difficult to find. I did not operate on the lateral rectus muscle at the same time. The patient still has some esophoria, but I made the incision, as I indicated on the lantern slide, at a downward and outward angle of about 20 degrees, keeping below the border of the external rectus muscle. Then, when the muscle was engaged, it was taken on two hooks, which were separated. Once in a while one will find the inferior oblique muscle tied up with the external rectus. If so, it is dissected away and one hook is pushed back to the insertion. Well toward the insertion I use a double-armed suture and cut the muscle beyond this. I then recede it to the distance believed necessary to secure the desired effect. The procedure is not difficult, and if any one thinks it is he might try it in the next case in which he is going to do an enucleation. Or, if one is going to do an operation in the lower outer quadrant of the globe, one might endeavor to engage the inferior oblique muscle with a hook when doing an external rectus muscle resection or recession; it does the inferior oblique no harm to pick it up and drop it back without

tenotomizing it, to see whether one can find it in about the same place. I have had no trouble finding it.

An infection has not developed in any of my cases. I do not see why infection should follow any muscle operation except as a rare accident. I have been more or less in touch with Dr. Berens' work at the New York Eye and Ear Infirmary, because some of the ophthalmologic surgeons there have been doing this operation at my suggestion and getting satisfactory results.

Dr. Frank Keil varied the procedure in 1 case. After the muscle was exposed it was drawn slightly to one side and the scleral suture taken at the desired distance along the line of the muscle before it had been displaced. The double-armed suture was passed through the muscle well toward the insertion. The muscle was then severed just beyond the suture. When the suture was tied, the muscle was replaced to the site of the scleral sutures.

This is not a bad idea, and I have suggested it to those surgeons who were afraid to perform the operation. I have done it many times and had no trouble. The surgeons at the New York Post-Graduate Medical School and Hospital do it frequently.

Effect of Mydriatics on the Intraocular Pressure in So-Called Primary Wide Angle Glaucoma. Dr. Peter C. Kronfeld, Dr. H. Isabelle McGarry (by invitation) and Dr. Homer E. Smith (by invitation), Chicago.

As the counterpart to narrow angle glaucoma, which since the advent of gonioscopy has become a well understood and sharply defined entity, wide angle glaucoma denotes the various forms of so-called primary glaucoma in which the intraocular pressure is abnormally high in the presence of a grossly normal, unobstructed chamber angle (except for occasional pigment infiltration of the trabeculum). In eyes which probably had wide angle glaucoma H. Köllner (*Arch. f. Augenh.* **88:** 58, 1921) showed that the intraocular pressure was as a rule not demonstrably influenced by the administration of mydriatics.

The present study represents a repetition of Köllner's work with the special aim of correlating the effect of homatropine on the intraocular pressure when the gonioscopic picture and other features are apparently characteristic of wide angle glaucoma. The results permit sharper definitions of those forms of so-called primary glaucoma which may be "provoked" by mydriatics.

DISCUSSION

Dr. S. Judd Beach, Portland, Maine: Dr. Kronfeld mentioned the report by Holt and me on dilation glaucoma at last year's meeting. His paper represents another step in running down the etiologic elements in this disturbance. Besides the narrow chamber angle, usually indicated by shallowness of the chamber, the endocrine glands are implicated, as shown by the overwhelming predominance of female patients. Some other factor is still unknown. Hans Barkan suggested the menstrual cycle. That something of this kind is involved is indicated by the observation of Magitot on the erratic behavior of reactions to provocative tests. He said, in reporting a series of cases, that in the same case an agent that will precipitate an exacerbation on one afternoon may have no effect whatever the following morning. Dr. Kronfeld's observations are of especial interest in supporting the preference of Scandinavian observers for the drinking test to the use of mydriatics in uncovering latent glaucoma.

Results of Desensitization in Tuberculous Iritis. Dr. E. V. L. Brown, Dr. Ernest E. Irons (by invitation) and Dr. S. L. Rosenthal (by invitation), Chicago.

This article was published in full in the December 1942 issue of the Archives, page 1028.

Experimental Studies of Ocular Tuberculosis: VII. Effect of Desensitization with Tuberculin in Experimental Ocular Tuberculosis. Dr. Alan C. Woods and Dr. Earl L. Burky, Baltimore (by invitation).

This article was published in full in the March issue of the Archives, page 369.

DISCUSSION OF PAPERS BY DRS. BROWN, IRONS AND ROSENTHAL AND BY DRS. WOODS AND BURKY

Dr. Allen Greenwood, Boston: I should like to say that during the past twenty-five years at least I have always followed the method of desensitization in treating tuberculous eyes, and I shall continue to so do. I am positive that I have had results from the procedure.

Dr. E. E. Irons, Chicago: In view of the newness of this approach and our lack of knowledge of the therapeutic action of the fumes used, we proceeded very carefully; perhaps later we shall learn that we have been overcareful. However, until we know more of the possible effects we still feel that the dose should be regulated in the manner described in the paper. No doubt further experience by other investigators will throw additional light on this question.

With respect to the nature of the material contained in the fumes, we know that when the fumes are passed through a fritted glass filter, so that presumably no tubercle bacilli or fragments thereof can be carried through, they have the same effect on guinea pigs that the unfiltered fumes did. The distillate from these fumes concentrated thirty times does not neutralize tuberculin.

Dr. Alan C. Woods, Baltimore: I should like to say this in appreciation of Dr. Brown's and Dr. Irons' work. The proper methods for the use of tuberculin for desensitization are far from being known. Evidence is gradually accumulating that the intracutaneous method may be preferable to the subcutaneous method. There is a peculiar class of patients who cannot be desensitized. Even the briefest exposure to tuberculin produces violent reactions. It may be possible with histaminase to produce a negative phase in these patients so that they later can be given tuberculin.

While Dr. Brown's work requires a great deal of standardization before physicians will dare use it clinically, it may be the secret to the proper approach to desensitization. Possibly the alveoli of the lungs are the proper portals of entry. As I have already said to Dr. Brown, while one observation does not prove a point, nevertheless it gives one considerable encouragement to know that there are additional therapeutic possibilities.

Dr. E. V. L. Brown, Chicago: I wish to disclaim any credit for this work. I am only the ophthalmologist; the work is Dr. Irons.'

Allergic Keratoconjunctivitis. Dr. C. S. O'Brien and Dr. J. A. Allen, Iowa City (by invitation).

This article was published in full in the April issue of the Archives, page 600.

DISCUSSION

Dr. Francis Heed Adler, Philadelphia: In the office I use pontocaine hydrochloride altogether for local anesthesia and have encountered a number of cases of sensitivity to this drug. Last year I had the unpleasant task of enucleating an eye which I am certain was lost because of such sensitivity. The patient consulted another ophthalmologist for a cyst on his lid, and I believe pontocaine hydrochloride was used at that time. The patient stated that a local anesthetic was instilled and conjunctivitis developed. He returned to the ophthalmologist, who said he had pink eye. The conjunctivitis grew worse, and when he went back again he was given a prescription for pontocaine hydrochloride to put in the eye. A lesion appeared on the lid, and a dermatologist was called in, who made

a diagnosis of pompholyx. I believe that is an old-fashioned term for any vesicle on the skin—a contact dermatitis. The condition gradually grew worse; a corneal ulcer developed, and the patient was seen in consultation by a number of physicians in Philadelphia. He then went to New York and was seen by Dr. Knapp, who suspected that he was sensitive to pontocaine. By that time the eye was ready for enucleation. He went to Florida, where Dr. Black saw him. Finally he had a chronically inflamed, sightless eye, which I removed. One day after the enucleation he had considerable secretion in the socket. I wanted to paint the lids with an astringent, and I unwittingly instilled a drop of pontocaine hydrochloride in the socket. I washed it out immediately, and he knew nothing about it. He called me up in an hour saying that I had put something in his eye which had caused the same reaction he had before. I saw him immediately, and he certainly had such a reaction. Thus it was known that he was sensitive to pontocaine. I believe such sensitivity is much more frequent than is realized.

DISCUSSION

DR. WILLIAM TARUN, Baltimore: I have several colored slides, taken at different times, of a patient I saw in 1934 in consultation with one of the younger ophthalmologists in Baltimore. The patient, a physician, complained of having something in his left eye, for which a solution of pontocaine hydrochloride to be used four times a day had been prescribed. This treatment was supplemented by use of merthiolate and atropine sulfate. Ten days after the onset of the symptoms I was asked to see the patient and found that the subjective symptoms were severe pain, slight visual disturbance and marked lacrimation. The objective symptoms were swelling of the lids and numerous hemorrhages of the ocular and palpebral conjunctiva, with marked proliferation of the tissues on the upper tarsal plate, somewhat resembling acute trachoma. The cornea showed a slight membrane at the temporal limbus, but the cornea itself had a fairly good luster. The condition appeared to me to be due to some chemical irritation—I must confess I did not suspect pontocaine. It occurred to me, however, that it might be due to merthiolate or emetine hydrochloride, for I had observed a case of amebic dysentery in which the latter had been prescribed a few days before the onset of ocular symptoms.

Since I had never employed merthiolate or pontocaine the use of these was immediately discontinued, and 0.5 per cent solution of phenacaine hydrochloride was substituted. Cold compresses and atropine were also suggested. Believing that the merthiolate and emetine hydrochloride were responsible, I instilled in a rabbit's eyes both of these drugs for a period of five days, but no change other than a slight conjunctival irritation resulted. Culture of material from the conjunctival sac was positive for Pneumococcus, and a solution of ethylhydrocupreine hydrochloride was prescribed. This, however, seemed to add fuel to the fire, and its use was discontinued.

In spite of treatment, the membrane continued to form in a concentric manner, as shown in the first slide. A section was removed, which, as reported by a pathologist of the University of Maryland, showed numerous epithelial cells. As the patient's condition became desperate, I asked Dr. Jonas Friedenwald to see him, and he expressed the opinion that it might be due to cocaine instillations, but these had not been used. He also suggested that the membrane be allowed to form completely over the cornea. As shown in the second slide, the cornea was completely covered with membrane except for a small central area. After about three weeks the eye became quiescent, with the formation of a slight haziness of the cornea and a reduction in the vision to 20/30. I had previously performed refraction for this patient on a number of occasions. There was moderately high myopia with the visual acuity corrected to 20/15 in each eye.

About three years later he returned complaining of a lump on his lower right lid. This proved to be a chalazion. In view of the fact that cocaine usually dilates the pupils and causes a diminution in vision, I suggested the use of pontocaine

hydrochloride solution. This was instilled several times. The lower lid was kept everted so that the lesion would not affect the entire cornea, and the cyst was opened and curetted. The patient was given a solution of sodium borate and instructed to use cold compresses. Later in the day I received a telephone call stating that he was suffering a great deal of pain, and, since he was of a somewhat nervous temperament, codeine was given for relief of the pain. The following morning the lower lid was swollen, and on the lid and ocular conjunctiva there were numerous hemorrhages; the cornea showed a slight loss of luster and stained readily with fluorescein, and he was given phenacaine hydrochloride to use every hour. Within a few days he made a complete recovery, with no loss of vision. I have no doubt that this was definitely a case of sensitivity to pontocaine.

Dr. Wilmer, some years ago, reported before this society a series of 500 cases in which pontocaine had been used, without a single instance of sensitivity. I must say I was misled by his report, and did not suspect pontocaine at this time. In the foreign literature a number of cases have been reported, but to my knowledge only 1 case in the United States. I found this report in the ARCHIVES after observing my case. Investigators, however, have proved a fact which should be borne in mind, i. e., that local anesthetics bear a certain relation to the tissues: The more rapid the effect of the anesthetic, the greater is the destruction of tissue. I am confident that nothing will take the place of cocaine and phenacaine hydrochloride in ophthalmic operations.

DR. F. H. VERHOEFF, Boston: My experience agrees with that of Dr. O'Brien, except that I believe I have seen cases of severer reactions than he has described. I recall particularly a case of sensitivity to atropine. The patient knew she was sensitive to atropine, but did not mention the fact. As a result of instillation in one eye of not more than 2 drops she lost the eye. She had a tremendous dermatitis. Her face looked as though she had erysipelas; she had a keratitis which went on to complete ulceration of the cornea, and I proved that it was due to atropine. I asked the intern to test her, and he injected 1 per cent atropine sulfate solution into the skin of her arm. As there was no reaction in twenty-four hours, he then injected a 2 per cent solution in the same arm. In another twenty-four hours the whole arm was a mass of inflammation. I recall 2 later cases of large ulcers of the cornea following the use of atropine. The patients came in with the ulcers and were still using atropine. When they discontinued use of the this drug the ulcers cleared up promptly, a fact which proved that they were due to atropine. In vernal catarrh one rarely sees corneal involvement, but the same type of ulcer does sometimes occur in this condition. The ulcers are characteristic. They may be large and may encroach on the pupillary area. The ulcers which Dr. O'Brien described are not serious and heal without causing loss of vision.

In connection with pontocaine, I had a patient on whom I used it when taking the intraocular pressure, and she had a marked reaction after she went home. She came back and complained that it was the drops I had put in her eye that caused the disturbance. I used phenacaine hydrochloride the next time, and she did not have any reaction. The next time I forgot and used pontocaine and she had another reaction. I believe that happened once more. Then I told her that if she ever had the reaction again it would be her own fault, because she should remind me not to use pontocaine.

DR. JOHN GREEN, St. Louis: Some years ago I was consulted by a woman who had had conjunctivitis for a week or more. She had been in the charge of a colleague, who had used ordinary measures without improvement. For the first few days my treatment was equally unsuccessful. One morning she volunteered the information that every time she wore a certain fur coat a facial eruption resembling acne developed. This suggested that the coat might have some bearing on the ocular condition. The patient was referred to a dermatologic colleague, who said: "This case is similar to several I have encountered recently; some women who wear iron-dyed fur coats have a cutaneous eruption, often associated

with conjunctivitis." After that the cure was simple. On request of the dermatologist, the furrier exchanged the fur coat for another that did not contain the iron dye. The patient promptly recovered without local medication.

Last December, as a woman was smoking a cigaret, some one jarred her elbow and cigaret ashes dropped into her eye. A small central corneal denudation developed. The pain was not severe. The lesion healed in a few days without the use of local anesthetics. Three months later, while she was shopping, the pain returned. She appeared at the office with a central superficial corneal lesion. There was no foreign material. The pain that day and the next was intense, and she was given 0.5 per cent pontocaine hydrochloride solution to use as frequently as necessary. On the third day I was startled to find an intense edema of the eyelids which extended to the cheek. A patch test with pontocaine hydrochloride gave a strongly positive reaction. Substitution of 1 per cent phenacaine hydrochloride was followed by prompt subsidence of all signs of the allergic reaction.

Dr. Alan C. Woods, Baltimore: My experience with such corneal and conjunctival lesions has been similar to that described by Dr. O'Brien. With regard to the detection of the specific allergen, there are one or two points of practical interest. Sensitivity to the inhalants, foods and bacterial toxins is best detected by the scratch test. Sensitivity to drugs can best be detected by the patch test. The detection of a local conjunctival or other ocular sensitivity can usually be carried out safely by instillation in the eye of extremely weak dilutions of the suspected allergen to provoke a local reaction. As to sensitivity to pontocaine, I believe the situation is not so black as it has been painted. While I have found sensitivity to butyn and atropine to be fairly common, sensitivity to pontocaine has in my experience been comparatively rare. Among a great number of cases in which pontocaine hydrochloride has been used as a local anesthetic, I have noted only 3 cases of sensitivity during the last three or four years. The mechanism of this sensitivity has been clearly worked out. Landsteiner, experimenting with guinea pigs, found that animals could not be sensitized to arsphenamine but could be sensitized to a mixture of guinea pig serum with arsphenamine. This observation applied also to various heavy metals and to silk, the mixture apparently denaturing the native protein.

Apparently this is what occurs in the eye: The patient is not sensitive at first, but with the action of the tears on the alkaloid a foreign protein is formed to which a sensitivity develops. That may be the reason, as Dr. O'Brien has pointed out, that in many cases the sensitivity is a local one and is difficult to detect unless weak dilutions of the allergens are applied directly to the conjunctival sac, the strength being increased until a local reaction is obtained. I believe that if this procedure is done carefully it is safe, and it is sometimes the only method by which one can demonstrate a specific allergic response.

Dr. William H. Crisp, Denver: In 1 or 2 cases of surgical intervention I observed a distinct edema of the conjunctiva and lids after use of 1:5,000 merthiolate ophthalmic ointment.

Dr. Eugene M. Blake, New Haven, Conn.: Will Dr. O'Brien say something about nupercaine, which I have used many times a day for at least ten years, and from which I do not think I have seen any such reaction?

Dr. Sanford R. Gifford, Chicago: I would just make a suggestion which may help in the prevention of induced reactions such as Dr. Verhoeff described. I have given butyn to patients I knew were sensitive because I had forgotten their sensitivity, but I now have put on every sheet of such patients' records, in red type, "No butyn" or "No pontocaine."' Even then I forget at times, and I always tell the patient to remind me not to use these drugs.

Dr. C. S. O'Brien, Iowa City: I am sure the discussion has been more interesting than the paper. I knew that cases of sensitivity were being encountered, but I believe it is well to bring them to attention occasionally.

In answer to Dr. Blake, we have not used nupercaine hydrochloride.

I am in agreement with Dr. Woods's discussion except that I have found that pontocaine hydrochloride has produced a number of such inflammations of the lids and conjunctiva. As a consequence, while I believe it is a good anesthetic, I would rather not use it. Our experience differs somewhat from that of other ophthalmologists, perhaps. Also, apropos of Dr. Woods's discussion, we used weak solutions of these drugs in the conjunctival sac, as stated in the paper.

Corneal Vascularization Problems. Dr. Derrick Vail, Cincinnati and Dr. K. W. Ascher, Cincinnati (by invitation).

In the conjunctivoscleral wedge a more or less extensive meshwork of vessels is normally present. Vascular arcades are given off which enter the transilluminable part of the limbus, so that their final loops seem to be situated in corneal tissue, which is merely the conjunctivoscleral wedge. Usually the venous return takes place separately for each loop by its own efferent limb, but often all or almost all blood returns by anastomosing veins which run concentrically with the limbus. For these vascular features the term "concentric collaterals" is proposed.

Concentric collaterals are engorged parts of the preexistent limbal meshwork.

These vascular anastomoses occurred in 13.3 per cent of persons with a manifest, subclinical or suspected deficiency in different vitamins observed in the Nutrition Clinic of Dr. T. D. Spies in Birmingham, Ala. They occurred in a much higher percentage in the ophthalmic clinic of the Cincinnati General Hospital.

Concentric collaterals should not be mistaken for corneal vascularization.

Any kind of long-standing engorgement in conjunctival vessels may result in the formation of concentric collaterals. They probably are due to a hindrance of venous outflow and probably are a kind of collateral circulation leading to the conjunctival veins in the horizontal meridian because of overcrowding in the original venous system. The dilatation is probably connected with cellular changes and not due entirely to stretching of the vessel walls. This fact interferes with an early reduction of the collaterals once they are formed; the dilatation of these vessels persists after disappearance of the provoking cause.

All patients in one group showing concentric collaterals had signs of or gave a history of repeated attacks of conjunctivitis; none of them was free from signs of chronic conjunctivitis; some of them were addicted to alcohol. Pingueculas and hyalin deposits were frequently found in the bulbar conjunctivas of these patients, even the younger ones. A relation between the severest conjunctival changes and the location of the concentric collaterals seemed to be present.

DISCUSSION

Dr. Alexander E. MacDonald, Toronto, Canada: My introduction to riboflavin deficiency disease was in a physician from the Connaught Laboratory of Toronto. He had been in the southern states and had been seen by Dr. V. P. Sydenstricker. I had not seen the vessels in his cornea, possibly because I looked only at the central area with the slit lamp. I have examined the limbus many times for slowing of the circulation in retinitis pigmentosa, and even now, after hundreds of examinations in this region, I have difficulty in locating the exact boundary of the limbus. Three different limbal regions must be recognized. Clinically one recognizes the line of junction of the sclera and the cornea. Under the microscope, pathologically the area measures at least 1 mm., extending beyond the limit of Bowman's membrane, where the epithelium develops an entirely different form, with papillae. With the slit lamp there is still another limbus, which must be further defined, and it is in connection with this area that one encounters difficulty in making a diagnosis of ocular ariboflavinosis from the invasion of the cornea by blood vessels. When Dr. Sydenstricker was in Toronto two months ago, he saw both patients represented by these slides. [Slides of the limbal regions were shown.] In the drawings the artist showed the beam in the cornea and the level of the vessels. The vessels, as may be seen, were superficial, with fragmentation

of the circulation in the vessels as they passed forward into the cornea. The venous return loop was deeper, as were the vessels tangent to the limbus. Both patients lost much vision in one eye.

Ariboflavinosis is a modern diagnosis, but riboflavin deficiencies are not at all modern, nor is corneal vascular invasion. Recently reviewed records of 100 pathologic ocular examinations made in 1936 showed that vessels invaded the cornea in 37 cases, and it is not likely that in all these invasion was due to riboflavin deficiency. The disease is often of long duration and may be serious. Many ophthalmologists have prescribed riboflavin for patients suffering from recurring lesions of the cornea, ulcers that remained over extended periods, typical cutaneous eruptions, and so on, and the improvement with 5 mg. of riboflavin a day is amazing. The only riboflavin available for intravenous use in Canada is combined with nicotine acidamide, 4 mg. of riboflavin and 200 mg. of nicotine acidamide, and I have not used it frequently.

The second lantern slide showed another type of corneal vascular invasion, which Dr. Sydenstricker believed was due to advanced riboflavin deficiency. The patient had recurring ulcers due to his being on a "relief" diet, which is good but deficient in riboflavin. I am not particularly satisfied with these drawings, but they will illustrate the difficulties encountered in considering for comparison this debatable region. However, it is necessary that different groups of investigators compare their findings on this important subject.

DR. K. W. ASCHER, Cincinnati: I should like to ask Dr. MacDonald whether his first picture represents an entirely clear cornea, or whether there were some corneal opacities or scars.

DR. ALEXANDER E. MACDONALD, Toronto, Canada: There was a very faint nebula.

DR. K. W. ASCHER, Cincinnati: That is interesting in proving that some condition preceded the proliferation of the vessels. I think there is no difference in our opinions except that I want to stress the fact that there is never a real corneal vascularization without a preceding corneal disease.

I should like to add a slide showing the frequency of concentric collaterals in the patients observed in Birmingham, Ala., and those in Cincinnati. Concentric collaterals occurred in about one half of all Cincinnati patients studied, whereas they occurred in only 14 per cent of the Birmingham patients, who were from the Nutrition Clinic of Dr. Spies, who studies patients with different kinds of vitamin deficiencies. In Cincinnati the patients were asked about their nutritional habits and were placed in three groups, as receiving very good, good and poor diets. In the group receiving poor diets there were 11 patients with concentric collaterals and 17 without; in the group receiving good diets there were14 patients with concentric collaterals and 10 without. This distribution, in my opinion, contradicts the idea of a nutritional cause of the concentric collaterals. Even the occurrence of concentric collaterals in the individual patient was not linked with nutrition; for instance, there were 10 patients with concentric collaterals in the group receiving good diets and only 5 in the group receiving poor diets. Only one eye was involved in 4 patients receiving good diets and in 4 receiving poor diets.

This is only a preliminary study on 69 patients selected at random in the ophthalmic clinic of the Cincinnati General Hospital. A later series might have another distribution. But the patients in Birmingham numbered more than 640, and they came from among patients with more or less severe deficiency diseases—some with manifest pellagra or with beriberi—and in spite of this fact only 14 per cent had concentric collaterals.

Local Sulfonamide Therapy of Catarrhal Conjunctivitis with Sulfonamide Compounds. DR. PHILLIPS THYGESON AND DR. ALSON E. BRALEY, New York (by invitation).

This article was published in full in the May issue of the ARCHIVES, page 760.

DISCUSSION

DR. SANFORD R. GIFFORD, Chicago: Dr. Thygeson's excellent work on conjunctivitis has stimulated the making of exact diagnoses in cases of the chronic form of this disease. I believe that this was a neglected field of ophthalmology for many years, until Dr. Thygeson, through the use of the sulfonamide drugs, brought about a realization of the importance of making an etiologic diagnosis. I have been following as well as I could a series of cases in which I have been using sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) locally. I have used this drug chiefly in cases in which I could make the diagnosis of staphylococcic conjunctivitis from cultures with mannitol-containing mediums in which there were strains of staphylococci which fermented mannitol. When cultures are difficult to obtain (some ophthalmologists may not have facilities for making them in their offices) the cases in which one would make a tentative diagnosis of staphylococcic conjunctivitis are those in which conjunctivitis is associated with chronic blepharitis, recurring styes and filtrates appearing around the limbus. I have had such a condition myself; so I have been especially interested in it. I arrived at the International Congress in Cairo with the largest stye on record and was very much humiliated. The treatment I have used is something like that which Dr. Thygeson describes, except that I have found it inconvenient to use ointment during the day. Most of my patients are greatly inconvenienced by it, and I have used a 3 per cent sodium sulfathiazole solution five or six times during the day and a 5 per cent sulfathiazole cream at night. A good many patients have responded well.

I have also encountered, as Dr. Thygeson has, cases of allergy to sulfathiazole, in which just when one believes the patient is perfectly well he comes in with an attack which was apparently precipitated by the treatment. At least, one has no way of knowing whether it was a recurrence or a result of the treatment except by checking with cultures. If cultures are negative some time after the drug has been used, one can presume that the attack was the result of sensitization and should discontinue the use of sulfathiazole therapy, use a mild alkaline wash and see whether the condition does not clear up.

The question is, How long can one use sulfathiazole before sensitization is likely to occur? I seldom use it longer than a month, and I then change to a mild alkaline solution to keep the conjunctiva clean. In some cases I have carried out Dr. Thygeson's previous suggestion of using staphylococcus toxoid with sulfathiazole.

Precancerous Melanosis and the Resulting Malignant Melanoma (Cancerous Melanosis) of the Conjunctiva and Skin of Lids. DR. ALGERNON B. REESE, New York.

This article was published in full in the May issue of the ARCHIVES, page 737.

DISCUSSION

DR. ALEXANDER E. MACDONALD, Toronto, Canada: In a series of 100 malignant pigmented tumors at the Banting Institute, 1 distinctly different in structure was encountered. There was a tendency to formation of glandlike structures, all the cells of which were heavily pigmented, so that the term melanotic carcinoma was justified. All other tumors in the series were of the sarcoma type.

The patient, a printer aged 60, had noticed a dark spot at the edge of the lower lid and believed that it was printer's ink in his eye.

Before exenteration of the orbit pigmented masses were present on both upper and lower lids, possibly owing to transplantation, as the canthus regions were clear of tumor cells.

The first lantern slide showed a vertical section of lids and globe *in situ*, with the heavy pigmented areas in both lids. The second slide showed a high power

magnification of the masses of pigmented cells arranged in glandlike form. Thus it seems that the conjunctiva may be the seat of melanotic carcinoma, and the use of this term is justified rather than the noncommittal designation malignant melanoma.

Dr. S. Judd Beach, Portland, Maine: In one of Dr. Reese's cases—and I am under the impression it was that of a patient I saw with him—there was a history that after an acute infection a recession took place not only in the melanosis of the eye but in a pigmented mole on the body. I should like to know whether he has any comment to make on the significance of this history.

Dr. Theodore L. Terry, Boston: In using an ultraviolet lamp with an ultraviolet filter one often finds that lesions containing melanin appear to be considerably larger, apparently resulting from fluorescence of "premelanin" in a true melanotic color. This is more striking with the mercury vapor lamp than with the carbon arc lamp.

Dr. Algernon B. Reese, New York: Dr. MacDonald's case seems to belong to the group discussed here.

Dr. Beach mentioned the spontaneous regression of a pigmented mole elsewhere in the body after an acute infection in a patient we saw together. I do not remember the acute infectious incident, but the disappearance of a pigmented mole in the preauricular region occurred at the same time.

Dr. Terry's mention of his observation concerning the fluorescence of these lesions is very interesting.

Metastatic Orbital Infection: Report of a Case. Dr. Frank E. Burch, St. Paul.

In the case presented, a staphylococcic septicemia, emanating from a furuncle with metastatic foci in the chest, hip and ankle, produced phlebitis of the orbit. Subacute exophthalmos with alarming evidence of thrombophlebitis of the orbital veins without signs of infection in the accessory sinuses led to exploration, drainage and ultimate recovery of the patient from the cellulitis. Sulfathiazole was of value in saving the patient's life as well as in controlling the local infection but without operation could not relieve the abscess of the orbit.

DISCUSSION

Dr. Alexander E. MacDonald, Toronto, Canada: There have been two important advances in the treatment of severe orbital infection, and complications formerly met are now rare. This preparation [a slide was shown] dates back to 1926 and shows a large orbital abscess from a celloidin section of the orbital contents. The hematoxylin stain picks out the masses of pus cells to the temporal side of the optic nerve. The patient was a woman aged 32 who had three teeth extracted from the right side of the lower jaw. Three days later she was admitted to the hospital with a swollen right cheek. In three days her right globe became proptosed and fixed and the lids swollen. The right cavernous sinus was drained, but the left eye became fixed and proptosed, and death ensued in one week.

The Staphylococcus aureus infection apparently went by direct extension through the pterygoid plexus, orbital veins and cavernous sinus to the left orbit.

The section shown by lantern slide demonstrated the abscess of the orbit and the thrombosed cavernous sinus. A clouding of the posterior part of the vitreous appeared when the globe became fixed, and the retinal veins were greatly enlarged. This picture of rapid extension of infection, it seems, can now be prevented by use of heparin to stop thrombosis and of the sulfonamide compounds to control the infection.

Dr. Eugene M. Blake, New Haven, Conn.: On March 21, 1942 I saw a patient with an infection similar to that reported by Dr. Burch. A boy aged 15,

of Italian extraction, was sent to me because of increasing prominence of the left eye of two months' duration. The symptoms began with sudden diplopia while he was observing a motion picture. There were an exophthalmos of 4 mm. and decreased motility, especially in outward rotation. Because of severe headaches present over the left eye and extending back to the occiput, several attacks of vomiting, absence of fever and absence of redness in the eye, a neoplasm was at first suspected.

Later the father of the patient stated that just before the onset of the exophthalmos the boy had had two boils on the back of the neck and had squeezed them, after which he had a chill.

The patient was sent to the hospital for study and possible operation. Physical examination, except for the ocular findings, gave essentially negative results. There was slight coryza, but no evidence of disease of the accessory sinuses. The teeth were good. The tonsils were enlarged, submerged and diseased. The pupils were equal and reacted normally. The fundi were normal except for slight distention of the veins of the left eye. Roentgenograms revealed no evidence of tumor of the orbit or sinus disease. The white blood cell count was 16,300; lumbar puncture showed a pressure of 150 mm.

After the patient's entrance into the hospital there was a somewhat rapid increase in the exophthalmos, pain, headache and redness of the globe. The boy was prepared for a Krönlein operation in case one should be necessary. However, an incision into the orbit between the globe and the lateral wall of the orbit was followed by evacuation of thick pus and subsidence of symptoms. Culture disclosed a hemolytic streptococcus (Streptococcus albus) and a nonhemolytic streptococcus. The level of sulfadiazine (2-[paraaminobenzenesulfonamide]-pyrimidine) was maintained at 9.7 to 10.4 mg. per hundred cubic centimeters before and after the operation.

The boy made an uneventful recovery, with disappearance of the exophthalmos, return of motility almost to normal and vision of 20/20.

Physiology of Aqueous in Completely Iridectomized Eyes.. Dr. Harold G. Scheie; Elinor Moore, Ph.D., and Dr. Francis H. Adler, Philadelphia.

This article was published in full in the July issue of the Archives, page 70.

Colored Reflex from Anterior Capsule of Lens Which Occurs in Mercurialism. Dr. Walter S. Atkinson, Watertown, N. Y.

The colored reflex from the anterior capsule is lusterless and rather homogeneous looking and can be seen with the aid of the slit lamp. Its color varies from a brownish gray to a deep rose-brown and it is thought to be a deposit of mercury.

It was observed in all patients examined who had symptoms of chronic mercurialism.

It is suggested as a diagnostic sign of mercurialism.

DISCUSSION

Dr. R. von der Heydt, Chicago: This is a very interesting field. The nearest analogous condition is chalcosis, in which there is a similar deposition. I think the term "deposition" is more nearly correct than reflex. In chalcosis there is a fine deposition of copper under the anterior lens capsule. This I was able to photograph (*Am. J. Ophth.* **18:** 1045 [Nov.] 1935). I had the opportunity of seeing the patient again after six years. All the copper had been absorbed. The incrustation of the vitreous with copper and the involvement of Descemet's area at the limbus, as well as the subcapsular copper-colored disk, had disappeared.

I should like to ask Dr. Atkinson what happened in his cases, whether the eyes still show the so-called reflex after so many years. I wonder why the reflex,

or the mercury, was not carried away. The narrow slit lamp beam might disclose where this deposition is. With copper the deposition is under the capsule, and it is not carried inward by the apposition of new lens fibers; so it must be in the lens epithelium.

Dr. Gifford has shown an eye with mercury in it, and I would ask if he has seen anything like this reflex in the lens. The eye had some metallic mercury carried into it by an explosion, and it remained there for a long time.

I want to thank Dr. Atkinson for this demonstration of ocular mercurialism.

Dr. John H. Dunnington, New York: Dr. Atkinson is to be congratulated on the discovery of this reflex in cases of mercurialism. It goes to show that those who observe, see. I am sure the reflex will prove to be a most important sign, for its frequent presence prior to the onset of other symptoms makes it of real diagnostic value. It was my good fortune to examine one of his patients, and the picture is most striking. The dull gray appearance of the lens with oblique illumination would certainly lead one to expect a reduction in visual acuity. Then, with the corneal microscope, to see the varying colors in different areas of the anterior capsule is most striking. To my mind the most outstanding feature was the marked increase in density of the reflex in the pupillary area. With the knowledge that such a deposit occurs in mercurialism, may one not expect similar reflexes to be found in chronic poisoning from some of the other heavy metals? However, so far as I have been able to learn, no descriptions of such reflexes have appeared in the literature.

I should like Dr. Atkinson to tell something of the experimental work he has been doing in an effort to produce the same type of reflex in animals exposed to mercury vapor, and I thank him again for describing this reflex.

Dr. Sanford R. Gifford, Chicago: The case I am about to describe is just a freak case, which will not throw any light on this interesting subject. I saw the patient with my assistant, Dr. W. H. Droegemueller. The man was walking under a neon light when it broke. Part of it struck his glasses, causing a slight cut in his cornea, and the mercury from the neon light actually got into his anterior chamber. Three little globules could be seen there. The wound was small and closed immediately. It produced a severe inflammation which was intractable to treatment. Unfortunately, the mercury was not removed at once, and later it was impossible to remove it. I have lost track of the case, but I believe the eye became practically blind and had to be removed because of the little globules of mercury, which looked innocent in the early stages. The inflammation became severe enough so that one could not detect the changes in the lens capsule which Dr. Atkinson described.

I had another freak case of mercurialism. The patient had been dropping mercurochrome (2 per cent) in his eye, when he became very much salivated. I did not know what was the matter with him, until I realized that he was instilling mercurochrome ten times a day and was actually absorbing enough to cause salivation.

Dr. K. W. Ascher, Cincinnati: This most interesting paper raises some questions about the chemistry and physics of the deposits. So far as physics is concerned, there is an analogy in a kind of spectacles which have been recommended to reduce glare. These are not polaroid glasses; they are constructed by depositing finest metallic particles over glass. An observer cannot see the eyes of a person wearing these glasses, but the latter is able to see very well and is not bothered by glare. This applies to the discrepancy mentioned by Dr. Atkinson between the objectively visible opacity of the lens and the good visual acuity in the eyes affected.

So far as chemistry is concerned, there is an interesting question raised by Dr. von der Heydt, namely, why in Dr. Atkinson's cases the appearance of the mercury deposits did not change during many years. Copper deposits finally may be removed, owing to the solubility of the deposited copper salt. The mercury

deposits are probably—I do not have any proof of this—insoluble compounds with lens proteins, and that may be the reason why they remain for a long time without being removed. One may even expect that later on, provided no further intoxication takes place, clear lens fibers will cover the strata of deposits.

There is another analogy to the mercury deposits, with regard to localization and aspect. The condition is rare, and, so far as I remember, only 1 case has been reported, that of Ollof and Siemerling, described about twenty years ago. The condition was Wilson's disease, and, besides the well known deposits in the periphery of the cornea, there were deposits of similar color in the anterior lens capsule. Similar deposits were found by Fleischer in the lamina vitrea of the choroid. These observations show that the elastic membranes of the eye may be a point of predilection for the deposition of very different substances.

DR. H. M. BURIAN, Hanover, N. H.: I should like to ask Dr. Atkinson whether he has any explanation as to why the periphery of the lens remains clear, or why the deposits are densest in the center.

DR. WALTER S. ATKINSON, Watertown, N. Y.: I am grateful for the interesting discussion of my paper, which has stimulated new thoughts regarding the problem.

Dr. von der Heydt asked about the duration of the reflex. Some patients had not worked with mercury for ten to twenty years, and the reflex was still present and vivid.

I had intended to include in the paper some matter regarding attempts to produce the reflex in rabbits and guinea pigs, but the results were disappointing and proved nothing. In some experiments the animals were placed in a cabinet each day for eight hours, but it was difficult to regulate the mercury content of the air at a uniform temperature and maintain proper ventilation. Some of the animals died of what appeared to be acute mercury poisoning and asphyxia, and others died of unknown causes. In other experiments the mercury was heated outside of the chamber in a closed vessel and the vapor carried to the chamber through a pipe. A temperature of 25 to 30 C. was maintained in the chamber, with adequate ventilation.

The concentration of mercury vapor was determined by an instrument designed by Swisher (research laboratory, General Electric Company) on the principle of the Nordlander instrument. With this instrument a concentration of 1 part of mercury vapor to 100,000,000 parts of air may be determined with an eight hour exposure.

One rabbit has survived four hundred and seventy-one hours in the chamber with the concentration of mercury averaging approximately 2 mg. per cubic meter of air. A faint gray reflex is beginning to be visible. When this becomes more pronounced, it is hoped by microscopic and chemical examination of the lenses to learn more about the exact location and form in which the mercury is deposited in the lenses.

Dr. Burian has asked why the deposits are centrally located. The iris seems to protect part of the lens, but just why more mercury is deposited at the center is difficult to explain.

Again I want to thank the members who have discussed this paper so interestingly.

Fibroblastic Overgrowth of Persistent Tunica Vaculosa Lentis in Premature Infants: II. Report of Cases—Clinical Aspects. DR. T. L. TERRY, Boston.

This article was published in full in the January issue of the ARCHIVES, page 36.

DISCUSSION

DR. RALPH I. LLOYD, Brooklyn: This is the first case to come to my attention in which this condition was bilateral. A case in which it is unilateral has been under my observation for about fourteen years. The patient was 4½ months old

when first seen, and a diagnosis of pseudoglioma was made because the opacity was at the posterior surface of the lens; it was cold gray (not yellow-white); there was a vessel carrying blood, and there was some pupillary response. Although a diagnosis of glioma had been made and immediate enucleation advised, the patient has been under observation since. This eye is evidently smaller than its fellow; the side of the face and the bony orbit are smaller, and the eye is farther back. The argument for retaining the eye of a child under these conditions is that further development of the orbit will occur. In any case in which there is the slightest doubt as to malignancy and the eye is without vision, this argument has no weight. If this particular eye had been sacrificed in infancy (if the diagnosis had been doubtful) there would have been no loss and only the inconvenience of an artificial eye. Microslides in another case showed the mass of tissue on the posterior surface of the lens and a large persistent hyaloid artery attached at the usual place. The second set of slides are from a case of Dr. H. F. Whalman, of Los Angeles. In addition to the mass on the back of the lens and the persistent hyaloid artery, the retina is totally detached and encloses the hyaloid stalk like a shroud. The cause of the detachment in small children is not known, but the anomaly is a recognized type of pseudoglioma. Some years ago, at the Royal London Ophthalmic Hospital, 24 eyes were removed with a diagnosis of glioma, and of the group, 7 showed developmental defects of this type.

Dr. Parker Heath, Detroit: The approach to this problem by Dr. Terry is highly commendable. He discusses largely the clinical phases, but he has also conducted a series of studies along experimental and embryologic lines and has made a search of the literature. To me his study is an outstanding contribution. No one ophthalmologist sees this anomaly often enough to be very sure of himself clinically, and I believe all should contribute their own material to the studies of Dr. Terry, so that he may have a large pool for study.

On the screen is a section of an eye which came to the Wayne laboratory recently. The case was of the monocular variety of the defect, except that the other eye had a curious anomalous congenital arrangement of vessels on the nerve head and persistent glial tissue—so-called Bergmeister's papilla—apparently a rather large mass of tissue partly on the nerve head. The specimen is poorly fixed, unfortunately; the retina is obviously detached, and the persistent hyaloid artery, covered with grayish material, is seen at the temporal border. According to the physician who sent the specimen in, the mass was continually enlarging; so he removed the eye, and justifiably. The patient was a full term infant. The lens has partly dropped out, but one can see clearly the retina and the mesenchymal membrane. The next slide shows the pupillary end of it with the hyaloid artery and the detachment of the retina. As in Dr. Howard's case, these prolongations of fine fibrillae extend into the vitreous.

The next slide shows some hemorrhage and pigment migration and ingrowing vessels; the process is progressive. The retina showed pseudorosettes, similar to those in the case reported by Verhoeff in 1906, in which pseudorosettes containing fibrillary structures were present in a malignant tumor of the ciliary body. This seems a transitional type of anomaly, between bilateral involvement and purely monocular involvement and I feel sure that as evidence accumulates there will be more and more proof of inflammatory changes in the mesenchymal tissues. Indeed, Dr. Terry pointed this out when he spoke of the development of synechias. There are chronic inflammatory cells in some of these membranes.

The patients who have done relatively well—the few I have seen—have been those with the lens partly absorbed and disklike, and they have secured some vision through a window cut in this membrane with scissors, not with a knife. The radial extensions back through the vitreous are so potentially dangerous that any tugging on this mass would detach the retina if it had not been detached before.

One is therefore confronted with the dilemma of either performing early operation or leaving the patient alone, with the evidence at present in favor of late

treatment. The eyes are small; the retina is usually undifferentiated. Leaving the eyes alone may allow differentiation of the retina—a potential source of glaucoma—and the eyes have very little vision. There is no benefit from early operation from the standpoint of amblyopia, because the best vision one gets is below the level of the amblyopic eye.

DR. R. VON DER HEYDT, Chicago: This contribution to ocular pathology is the most important of recent years.

Dr. Terry has brought out the fact that the tunica vasculosa lentis, which is destined to absorption, may result in an overgrowth in premature infants. Usually premature infants in hospitals are watched as to whether they will live, not as to whether they have any abnormal ocular condition. I congratulate Dr. Terry on having discovered this condition in such infants.

I like the term "Mittendorf dots." It gives credit to Mittendorf, who first described these symmetric black dots on the back of the lens, although he did not know why they were there.

Dr. Terry's discussion was also very interesting with regard to how the hyaloid artery normally stretches and bursts. There is a beautiful slit lamp picture of that in nature's physiologic disposition of the remnant of the hyaloid artery. The stretching gives it the spiral shape.

In deference to the memory of the late Dr. Francis Lane, who was the predecessor of Dr. Georgiana Dvorak Theobald and the successor to Dr. E. V. L. Brown, I want to mention that his membership thesis to this society was a study on "Persistent Fibrovascular Sheath."

There is one point I wish to reemphasize which Dr. Terry brought out and which is important in differential diagnosis between the anomaly he discussed and glioma. A gliomatous mass may reach the back of the lens and can be seen as a vascular membrane; he drew attention to the fact that in a persistent fibrovascular sheath the blood vessels radiate from the center. This is not the case in retinoblastoma.

DR. SANFORD R. GIFFORD, Chicago: I had a case like the one Dr. Terry reported in which there was a little round mass on the back of the lens (exactly similar to that in a case Leach observed in Chicago). I enucleated the eye for probable retinoblastoma, and when I found out what the defect was, I looked at my record and found the notation that the cornea had measured 9 mm. on that side, as opposed to 11 mm. on the other side. Since then I have used the size of the cornea as a criterion in differentiating between this condition and glioma. I should like to ask Dr. Terry if it is not true that in nearly all cases of glioma the cornea is of normal size. Even if one is going to take the eye out, as Dr. Lloyd suggests (I do not agree with his suggestion), I believe one should endeavor to make a diagnosis. I have encountered 4 other cases, in which I have avoided removing the eye, which has remained fairly sightly, at least better than the result of enucleation.

DR. ROBERT H. COURTNEY, Richmond, Va.: Several years ago a young woman who had been in an automobile accident had a complete evulsion of the optic nerve. After the accident there was no bleeding or disturbance of the circulation. There was, however, a complete cone-shaped detachment of the retina, extending from the ora serrata to the macula and the disk. This shows that there can be a tremendous amount of stretching of the retina and of the vessels of the retina without any bleeding. This patient has been under my observation for a number of years, and there has been no evidence of deterioration of the retina during this time.

Abscess of Crystalline Lens. DR. RALPH O. RYCHENER and DR. EDWARD C. ELLETT, Memphis, Tenn.

Purulent infiltration of the lens often accompanies perforating injuries of the globe, the diagnosis usually being made by pathologic section after enucleation.

The literature was briefly reviewed and a case reported in which there was a primary abscess of the lens following the intraocular appearance of a foreign body. The report was illustrated by serial kodachrome photographs. Chemotherapy and paracentesis caused resolution of the purulent infiltration. The eye became quiet, with some retention of vision.

DISCUSSION

DR. FRANCIS HEED ADLER, Philadelphia: The ordinary crystalline preparations of the sulfonamide compounds cannot be injected with a hypodermic needle, as the crystals are too large. Dr. B. F. Souders, in my department, conceived the idea that these crystals might be broken up by sonic vibration, and one of the research chemists in the Johnson Foundation succeeded in doing this and in producing a microcrystalline form of the drugs. The importance of this was immediately recognized by the whole surgical division of the hospital, and the Smith, Kline & French Laboratories made a grant to the hospital for the study of these preparations. A report on the crystalline form of the drugs has already been made (Chambers, L. A.; Harris, T. N.; Schumann, F., and Ferguson, L. K.: The Use of Microcrystals of Sulfathiazole in Surgery, *J. A. M. A.* **119:** 324 [May 23] 1942). We have used the microcrystalline form in experimental intraocular injections and believe that it is of value. Some of the histologic sections, however, show changes in the retina which we believe may be due to the drug itself, and accordingly we are not advising intraocular injection at the present time. In desperate cases, such as those just reported, the microcrystalline form might be of some use.

At present its chief usefulness in ophthalmology seems to be in a lacrimal syringe for getting sulfonamide compounds into the lacrimal sac.

DR. WILLIAM CRISP, Denver: I am not clear as to the use of the crystals. Are they in solution?

DR. FRANCIS HEED ADLER, Philadelphia: The crystals are in suspension. They are small enough to go through the needle.

Cataract Complicating Corneal Scars After Perforating Ulcers. DR. BERNARD SAMUELS, New York.

This article was published in full in the April issue of the ARCHIVES, page 583.

DISCUSSION

DR. C. A. CLAPP, Baltimore: I should like to ask Dr. Samuels if there is any scientific proof for what I understood him to say, that the central subcapsular cells are nutritional and the peripheral ones germinal, and, if there is such scientific proof, just where the differentiation between these two portions exists.

DR. BERNARD SAMUELS, New York: In reply to Dr. Clapp's question, this paper deals with cataract from an anatomic rather than from a chemical standpoint. So far as metaplasia and abnormal products of the epithelial cells of the lens are concerned, as an exception an anterior subcapsular epithelial cell may produce a vesicular type of cell, such as is the characteristic abnormal product of a germinal cell at the equator. On the other hand, a germinal cell at the equator may produce a spindle-shaped cell, such as is the characteristic abnormal product of an anterior polar cataract.

Fields of Vision in Cases of Tumor of Rathke's Pouch. DR. HENRY P. WAGENER and DR. J. GRAFTON LOVE, Rochester, Minn. (by invitation).

This article was published in full in the June issue of the ARCHIVES, page 873.

DISCUSSION

DR. WALTER I. LILLIE, Philadelphia: The cases reported by Dr. Wagener emphasized strikingly that ophthalmologists are too timid in making an early diagnosis of prechiasmal and chiasmal lesions from the visual field defects. The visual changes occur early, and in 94 per cent of the cases the characteristic changes in the visual fields are present in one or both eyes. The fundus reflex may vary from normal to pallor of one or both disks. There may be simple optic nerve atrophy or choked disk. Choked disk is rare with lesions of the midfossa, and the absence of this fundus change should not rule out a space-taking lesion. Other examinations should be instituted early, including a complete roentgenologic and neurologic study. A Rathke pouch tumor has its anlage from rests of cells in the craniopharyngeal canal and occurs usually in young patients. A diminution of vision in one or both eyes is an early sign, and the patient usually consults an ophthalmologist first. When proper glasses do not improve central visual acuity to normal, careful perimetric field studies should be done. Only by this method can the early field changes, so characteristic of prechiasmal and chiasmal lesions, be noted. When these are found, a complete general and neurologic examination should be done and the patient referred as soon as possible to the neurosurgeon. The mortality rate is not high, and surgical intervention is the only means of effecting a relief or cure. If the lesion is untreated, blindness follows rapidly, and if the patient survives he becomes a public liability, and, from an economic standpoint, in states with blind pensions for the blind a greater tax burden will result.

DR. ALLEN GREENWOOD, Boston: I saw a number of these tumors with Dr. Harvey Cushing during his later years in Boston, and I was struck with the point Dr. Lillie has been stressing.

DR. HENRY P. WAGENER, Rochester, Minn.: I wish to thank the discussers for their comments and to stress the point that, as Dr. Lillie and Dr. Greenwood stated, the fields of vision are of primary importance in the diagnosis. It is not wise or necessary to delay surgical intervention in all cases until the development of positive roentgengraphic changes in the skull. Although it is commonly assumed that suprasellar calcification will be present in association with 85 to 90 per cent of craniopharyngiomas, in 7 of the present group of 29 cases the roentgenograms of the head were normal at the time of operation.

Tumor Formation at the Disk. Report of a Case. DR. W. E. FRY and DR. P. DE LONG, Philadelphia.

A tumor of the papilla was described from both the ophthalmoscopic and the pathologic point of view. The margins of the disk were raised about 1.5 D. in the lower nasal quadrant. All margins were hazy, and all appeared raised except that at the upper temporal quadrant. The retina became completely detached. Section of the eye disclosed a tumor mass within the papilla, separate from the choroid. The nuclei in this mass were enlarged and oval, with moderate variations in size. A small amount of pigment was present in some but not all sections.

DISCUSSION

DR. BERNARD SAMUELS, New York: This case reminds me of a case I observed a few years ago at the New York Eye and Ear Infirmary. One eye showed a whitish mass over the optic nerve. It was not certain whether it was a papilledema. As it appeared to be solid and had a globular outline, it suggested a conglomerate tubercle of the optic nerve. The eye was enucleated, and the entire mass was found to be made up of epithelial cells that did not seem to be characteristic of any gland in the body. A few months later the patient was placed in an insane asylum. Shortly afterward he died. A postmortem examination revealed that the primary tumor was a carcinoma of the stomach.

In another case the patient was referred by a laryngologist. He had had a pansinusitis for which a radical operation had been performed. In the choroid of one eye there were several whitish spots, slightly elevated and sharply defined. He was on his way to Europe, and soon after his arrival there he consulted Professor Siegrist, in Berne, Switzerland. By that time the second eye was involved. A diagnosis of bilateral miliary tuberculosis was made. He was placed in a hospital, where in a short time he died of what was diagnosed as pneumonia. An autopsy revealed that the primary tumor from which the ocular lesions were derived was located in the lungs.

These 2 cases demonstrate that the first clinical manifestation of a tumor elsewhere in the body may be found in the fundus of an eye.

DR. F. H. VERHOEFF, Boston: I saw the sections of this tumor, and I am sure that the diagnosis of malignant melanoma is incorrect. Sections showed areas of neuroglia proliferated from the retina, which had been folded up or injured in some way. The part of the growth that could have been the original tumor was not shown in the photographs. That part consisted of proliferating vessels and endothelium arising from them. Some of the pigment in the tumor seemed to arise from the retinal pigment epithelium, and the remainder was probably blood pigment. The nature of the pigment could have been determined by certain methods, but these were not applied. I am sure, however, that it was not pigment such as occurs in malignant melanoma. I think it is unfortunate that this tumor should get into the literature as a malignant melanoma of the papilla. In the first place, it was not a tumor of the papilla, but arose at the side of the papilla, and, in the second place, it was not a melanoma.

DR. WILFRED E. FRY, Philadelphia: I wish to thank Dr. Samuels for his discussion.

At the time Dr. Verhoeff was kind enough to look at the sections there were certain things I failed to bring out as well as I should have. The position of the tumor in the papilla does not seem to me very important. Certainly the papillary region was involved. I am aware that differences of opinion can exist as to the exact nature of the tumor. I had the specimen examined by several pathologists in Philadelphia, who considered the tumor a malignant one, and at least one of them regarded the pigmentation as important in the diagnosis. That was why we suggested that the tumor was a malignant melanoma.

Extrapapillary Coloboma. DR. RALPH I. LLOYD, Brooklyn.

Extrapapillary coloboma, a congenital and even familial defect, may be mistaken for tuberculous choroiditis, hereditary macular degeneration or idiopathic choroiditis. These lesions are also the basis of claims for blindness of traumatic origin and recent losses of vision by policy holders of life insurance with disability clause attached.

DISCUSSION

DR. R. VON DER HEYDT, Chicago: I should like to draw Dr. Lloyd's attention to another condition that might be included in the differential diagnosis as a vague possibility—a healed glioma. That sounds as though it may never occur. I refer you to an article by Axenfeld, who depicts such a case and diagnosed it so in Hirschberg's Zentralblatt (1916).

DR. T. L. TERRY, Boston: As usual, Dr. Lloyd has discussed a subject of considerable interest. The point he brings out, that unscrupulous persons have used the existence of congenital visual defects to obtain undeserved settlements from insurance companies, is increasingly important, as the settlement of industrial accidents is becoming a considerable and economic factor. An example of this general type came to my attention in connection with a former chauffeur who had been pensioned, for a time at least, when congenital color blindness was discovered. He had been advised that this color blindness was acquired. When his pension

was stopped, he consulted me, requesting that I furnish him with a statement to his former employer that his eyes were again normal in order that he might obtain from her a letter of recommendation enabling him to return to a former position.

Dr. Lloyd's illustrations are interesting and instructive. His discussion and terminology again bring up for consideration the possibility that the eye may rotate during development in order that the fetal fissure, which is classically located downward and inward, may turn somewhat and be represented in the new position by the nerve fiber raphe extending temporally from the macula through the fovea, or that accessory colobomas can exist extending toward the macula, as illustrated in the older textbooks.

Presentation of New Instruments

A Confirmation Test for Refraction. Dr. Conrad Berens, New York.

The confirmation test for the refractionist consists in use of two spheres or two cylinders, one plus and the other minus, mounted on one handle and so arranged that the examiner may check the patient's acceptance with great facility. This arrangement of lenses not only furnishes a means of rapidly checking the patient's answers but is almost an essential in the trial case unless the ophthalmologist has more than one set of trial lenses. The pairs of lenses which have been found to be most universally useful are the plus and minus 0.25 D. spheres and cylinders, but spheres and cylinders are available from 0.25 D. to 1.00 D.

The handle is round and knurled, 62 mm. in length and branched at one end to support lens rings for holding 38 mm. lenses. The handle is marked to show the strength of the lenses in diopters, and the lenses are also marked, the minus in red and the plus in white. In use, the plus and minus 0.25 D. cylinders are held in the right hand and the spheres in the left hand, and the accuracy of the correction is checked rapidly by placing the lenses before those in the trial frame and presenting first the plus and then the minus lenses merely by twirling the handle of the instrument. At times it is advantageous to superimpose the cylinders and spheres.

Candidates' Theses

Progressive Myopia: A Possible Etiologic Factor. Dr. Edwin W. Burton, Charlottesville, Va.

Endophthalmitis with Secondary Glaucoma Accompanying Absorption of the Crystalline Lens. Dr. Robert H. Courtney, Richmond, Va.

Further Observation on Autofundoscopy (Auto-Ophthalmoscopy of Eber: Purkinje Figure of Walker). Dr. Leslie C. Drews, St. Louis.

Herpes Zoster Ophthalmicus: Report of Cases and Review of the Literature. Dr. Ambrose Earl Edgerton, San Francisco.

Ocular Pathology of Methyl Alcohol Poisoning. Dr. Walter H. Fink, Minneapolis.

Transscleral Lacrimal Canaliculus Transplants. Dr. Glen Gregory Gibson. Philadelphia.

Experimental Study of Iridodialysis. Dr. George L. Kilgore, San Diego, Calif.

Use of Conjunctival Flaps in Cataract Extraction. Dr. Walter Moehle. Brooklyn.

Objective Strabismometry in Young Children. Dr. Maynard C. Wheeler, New York.

This article was published in full in the May issue of the Archives, page 720.

Book Reviews

Transactions of the Ophthalmological Society of Australia (British Medical Association). Published under the direction of the Editorial Committee. Volume III, 1941. Price, 7s 6d. Pp. 176. Sydney, Australia: Australasian Medical Publishing Company, Ltd., 1942.

The table of contents lists twenty-five excellent articles, covering a wide field in ophthalmology, presented at the third annual meeting of the Ophthalmological Society of Australia (British Medical Association), held at the Royal Australasian College of Surgeons, Melbourne, on Oct. 15, 1941. Among the subjects are vision in relation to aviation, lighting in industry and a survey of blindness. Perhaps the most original paper is on the association of cataract with German measles, by N. McAlister Gregg. In this article it is stated that in the first half of 1941 an unusual number of cases of congenital cataract were observed in Sydney. Similar cases were reported from widely separated parts of Australia. On closer investigation it was found that the condition occurred in the form of a mild epidemic in New South Wales, Victoria and Queensland. The total number of cases were 78, while the author's own cases came to 13. The babies were small, ill nourished and difficult to feed. The cataract was generally bilateral and was present at birth as a dense white opacity in the pupillary area. The pupillary reaction was sluggish, and it was difficult to dilate the pupil with atropine. The iris had an atrophic appearance. After dilatation a dense white opacity was present in the center of the lens and was surrounded by a zone of lesser density of smoky appearance. Nystagmus was observed in the older babies and in those whose treatment had been delayed. In 16 babies the lesion was monocular, and in 10 of these definite microphthalmos was present. General examination showed that a high percentage of the babies had a congenital defect of the heart consisting of pronounced patency of the ductus arteriosus. Search for a possible cause revealed that all but 10 of the mothers had suffered from a disease early in their pregnancy which was regarded as German measles. The epidemic form was supposed to have been particularly severe, with swelling of the glands of the neck, sore throat, involvement of some of the joints and well marked constitutional disturbances. Discission of the cataract was more difficult than usual, and absorption was slower than in the ordinary lamellar cataract.

ARNOLD KNAPP.

Astigmatismo, biastigmatismo y tablas de transformacion. By Prof M. Marquez. Pp. 126, with 30 illustrations. Mexico: 1943.

Professor Marquez' well known ideas about biastigmatism are extensively developed in this book. The first chapter deals with spherical refraction and the second with cylindric lenses and bicylindric combinations. In the following chapters the diagnosis of astigmatism by skiascopy and with cylinders is aptly explained. Then there is a comparison of the Marquez method with use of the ophthalmometer and subjective examination, on the one hand, and the ordinary methods, on the other. Marquez considers the use of the ophthalmometer to measure the curvature of the anterior surface of the cornea as important as the use of the ophthalmoscope. He always applies it in connection with the subjective method to determine the amount of biastigmatism.

The book ends with thirty-one pages of mathematical tables for converting bicylindric combinations into spherocylindric lenses and instructions on how to use them. The author asserts that, although by trigonometry and use of logarithms the conversion is not difficult, it is much more practical to use these tables, which he made in collaboration with Dr. Bustos.

MANUEL URIBE TRONCOSO.